Trying 3106016892...Open

Welcome to STN International! Enter x:x
LOGINID:ssspta1644pnh
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS 13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved
NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22	Nov 29	COPPERLIT now available on STN
NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 24	Nov 30	Files VETU and VETB to have open access
NEWS 25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26	Dec 10	DGENE BLAST Homology Search
NEWS 27	Dec 17	WELDASEARCH now available on STN
NEWS 28	Dec 17	STANDARDS now available on STN
NEWS 29	Dec 17	New fields for DPCI
NEWS 30	Dec 19	CAS Roles modified
NEWS 31	Dec 19	1907-1946 data and page images added to CA and CAplus

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:54:09 ON 15 JAN 2002

=> file medline embase biosis scisearch caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 10:54:28 ON 15 JAN 2002

FILE 'EMBASE' ENTERED AT 10:54:28 ON 15 JAN 2002

FILE 'BIOSIS' ENTERED AT 10:54:28 ON 15 JAN 2002

FILE 'SCISEARCH' ENTERED AT 10:54:28 ON 15 JAN 2002

FILE 'CAPLUS' ENTERED AT 10:54:28 ON 15 JAN 2002

=> s CETP

L1 3632 CETP

=> s l1 and cholesteryl ester transfer protein

4 FILES SEARCHED...
L2 2942 L1 AND CHOLESTERYL ESTER TRANSFER PROTEIN

=> s l2 and recombinant

L3 107 L2 AND RECOMBINANT

=> s l3 and human

3 FILES SEARCHED...
L4 90 L3 AND HUMAN

=> s l4 and vaccine

L5 2 L4 AND VACCINE

=> dup remove l5

PROCESSING COMPLETED FOR L5
L6 2 DUP REMOVE L5 (0 DUPLICATES REMOVED)

=> d l6 1-2 cbib abs

L6 ANSWER 1 OF 2 MEDLINE

2000482102 Document Number: 20436374. PubMed ID: 10978256.

Vaccine-induced antibodies inhibit **CETP** activity in vivo and reduce aortic lesions in a rabbit model of atherosclerosis.

Rittershaus C W; Miller D P; Thomas L J; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR

BIOLOGY, (2000 Sep) 20 (9) 2106-12. Journal code: B89; 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.

AB Using a **vaccine** approach, we immunized New Zealand White rabbits with a peptide containing a region of **cholesteryl ester transfer protein** (**CETP**) known to be required for neutral lipid transfer function. These rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits than in controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP** and support the concept that inhibition of **CETP** activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

1999:223038 Document No. 130:250711 Vector **vaccines** against cholesterol ester transfer protein for the treatment of atherosclerosis.

Needleman, Philip; Glenn, Kevin (Monsanto Company, USA). PCT Int. Appl. WO 9915655 A1 19990401, 99 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19366 19980917. PRIORITY: US 1997-934367 19970919.

AB Expression vectors for manuf. of antigenic fragments of **cholesteryl ester transfer protein** (**CETP**) that can be used to inactivate the protein are described. The protein plays a key role in the transfer of cholesterol from HDL to LDL and VLDL and inhibition of **CETP** synthesis can be used to prevent LDL and VLDL formation in the prophylaxis of atherosclerosis. Immunogens, inocula, DNA segments, and **recombinant** DNA mol. vectors useful for carrying out the invention are also disclosed. The use of antigenic fragments of rabbit **CETP** to raise autoantibodies in rabbits is demonstrated. Antibodies to three such peptides cross-reacted with **human CETP**. Rabbits vaccinated with these antigens showed a .apprx.10% increase in serum HDL. Antigens were manufd. as fusion proteins with hepatitis B core antigens in Escherichia coli, in a baculovirus system, and in mammalian cell culture.

=> d his

(FILE 'HOME' ENTERED AT 10:54:09 ON 15 JAN 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:54:28 ON 15 JAN 2002

L1 3632 S CETP
L2 2942 S L1 AND CHOLESTERYL ESTER TRANSFER PROTEIN
L3 107 S L2 AND RECOMBINANT
L4 90 S L3 AND HUMAN
L5 2 S L4 AND VACCINE
L6 2 DUP REMOVE L5 (0 DUPLICATES REMOVED)

=> s l3 and rabbit

L7 23 L3 AND RABBIT

=> dup remove l7

PROCESSING COMPLETED FOR L7
L8 7 DUP REMOVE L7 (16 DUPLICATES REMOVED)

=> d l8 1-7 cbib abs

L8 ANSWER 1 OF 7 MEDLINE
2000482102 Document Number: 20436374. PubMed ID: 10978256.
Vaccine-induced antibodies inhibit **CETP** activity in vivo and reduce aortic lesions in a **rabbit** model of atherosclerosis.
Rittershaus C W; Miller D P; Thomas L J; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR
BIOLOGY, (2000 Sep) 20 (9) 2106-12. Journal code: B89; 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.
AB Using a vaccine approach, we immunized New Zealand White **rabbits** with a peptide containing a region of **cholesteryl ester transfer protein** (**CETP**) known to be required for neutral lipid transfer function. These **rabbits** had significantly reduced plasma **CETP** activity and an altered lipoprotein profile. In a cholesterol-fed **rabbit** model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated **rabbits** than in controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP** and support the concept that inhibition of **CETP** activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS
1999:223038 Document No. 130:250711 Vector vaccines against cholesterol ester transfer protein for the treatment of atherosclerosis. Needleman, Philip; Glenn, Kevin (Monsanto Company, USA). PCT Int. Appl. WO 9915655 A1 19990401, 99 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA,

GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19366 19980917. PRIORITY: US 1997-934367 19970919.

AB Expression vectors for manuf. of antigenic fragments of **cholesteryl ester transfer protein** (**CETP**) that can be used to inactivate the protein are described. The protein plays a key role in the transfer of cholesterol from HDL to LDL and VLDL and inhibition of **CETP** synthesis can be used to prevent LDL and VLDL formation in the prophylaxis of atherosclerosis. Immunogens, inocula, DNA segments, and **recombinant** DNA mol. vectors useful for carrying out the invention are also disclosed. The use of antigenic fragments of **rabbit CETP** to raise autoantibodies in **rabbits** is demonstrated. Antibodies to three such peptides cross-reacted with human **CETP**. **Rabbits** vaccinated with these antigens showed a .apprx.10% increase in serum HDL. Antigens were manufd. as fusion proteins with hepatitis B core antigens in Escherichia coli, in a baculovirus system, and in mammalian cell culture.

L8 ANSWER 3 OF 7 MEDLINE DUPLICATE 1

97164895 Document Number: 97164895. PubMed ID: 9012657. Plasma kinetics of **cholesteryl ester transfer protein** in the **rabbit**. Effects of dietary cholesterol. McPherson R; Lau P; Kussie P; Barrett H; Tall A R. (Lipoprotein and Atherosclerosis Group, University of Ottawa Heart Institute, Canada.. rmcphers@heartinst.on.ca) . ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1997 Jan) 17 (1) 203-10. Journal code: B89; 9505803. ISSN: 1079-5642. Pub. country: United States. Language: English.

AB The plasma kinetics of **recombinant** human **cholesteryl ester transfer protein** (rCETP) were studied in six **rabbits** before and after cholesterol feeding (0.5% wt/wt). The rCETP, labeled with the use of the Bolton Hunter reagent, was shown to retain neutral lipid transfer activity. After intravenous infusion, labeled rCETP associated with **rabbit** lipoproteins to an extent similar to endogenous **rabbit CETP** (62% to 64% HDL associated). The plasma kinetics of **CETP**, modeled with the use of SAAM-II, conformed to a two-pool model, likely representing free and loosely HDL-associated **CETP** (fast pool) and a tightly apo (apolipoprotein) AI-associated (slow pool) **CETP**. The plasma residency time (chow diet) of the fast pool averaged 7.1 hours and of the slow pool, 76.3 hours. The production rate (PR) into and the fractional catabolic rate (FCR) of the fast pool were 20 and 10 times the PR and FCR, respectively, of the slow pool. In response to cholesterol feeding, **CETP** PR, FCR, and plasma mass increased by 416%, 60%, and 230%, respectively. There was a strong correlation (r = .95, P = .003) between the increase in **rabbit** plasma **CETP** and the modeled increase in **CETP** PR in response to cholesterol feeding, suggesting that labeled human rCETP is a satisfactory tracer for **rabbit** plasma **CETP**. **CETP** is catabolized by distinct pools, likely corresponding to an apo AI-associated (slow) pool and a free and/or loosely HDL-associated (fast) pool. Factors that alter the affinity of **CETP** for HDL would be predicted to result in altered **CETP** catabolism. The effect of dietary cholesterol on plasma **CETP** mass can be explained largely by the effects on **CETP** synthesis, consistent with the observed effects of cholesterol on tissue mRNA levels.

L8 ANSWER 4 OF 7 MEDLINE DUPLICATE 2

97376917 Document Number: 97376917. PubMed ID: 9233688. Modification of the N-terminal cysteine of plasma **cholesteryl ester transfer protein** selectively inhibits triglyceride

transfer activity. Kotake H; Agellon L B; Yokoyama S. (Biochemistry 1, Nagoya City University Medical School, Nagoya, Japan.) BIOCHIMICA ET BIOPHYSICA ACTA, (1997 Jul 12) 1347 (1) 69-74. Journal code: A0W; 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB An invariant cysteine residue is found at the N-terminus of **cholesteryl ester transfer protein** (**CETP**) isolated from plasma of humans, **rabbits** and cynomolgus monkeys. We previously reported the expression of **recombinant rabbit cholesteryl ester transfer protein** in yeast (Kotake et al., J. Lipid Res. 1996; 37: 599-605). The **recombinant CETP** secreted into the medium contains an altered N-terminal sequence but was fully capable of facilitating both cholesteryl ester (CE) and triglyceride (TG) transfer between lipoproteins. We investigated the importance of the conserved N-terminal cysteine of plasma **CETP** in the lipid transfer activity by chemical modification of the free sulfhydryl groups of the **recombinant CETP** and **CETP** from human and **rabbit** plasma. The unmodified forms of these **CETPs** had similar specific activities of CE and TG transfer. Neither 5,5'-dithiobis-(2-nitrobenzoate) nor N-ethyl maleimide altered the lipid transfer activity. In contrast, p-chloromercuriphenyl sulfonate selectively inhibited the TG transfer activity of both human and **rabbit** plasma **CETP**. The TG and CE transfer activities of the **recombinant CETP**, which lacks the N-terminal cysteine residue, was not affected. These results demonstrate that the N-terminal cysteine residue of both human and **rabbit** plasma **CETP** is free and is likely to be involved in the construction of a critical part of the active site of **CETP** that can determine the selectivity of the lipid molecule for the transfer reaction.

L8 ANSWER 5 OF 7 MEDLINE DUPLICATE 3

96292476 Document Number: 96292476. PubMed ID: 8728322. Expression and secretion of **rabbit** plasma **cholesteryl ester transfer protein** by Pichia pastoris. Kotake H; Li Q; Ohnishi T; Ko K W; Agellon L B; Yokoyama S. (Lipid and Lipoprotein Research Group, University of Alberta, Edmonton, Canada.) JOURNAL OF LIPID RESEARCH, (1996 Mar) 37 (3) 599-605. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB The **rabbit cholesteryl ester transfer protein** (**CETP**) was expressed in the methylotrophic yeast Pichia pastoris by introducing the **CETP** cDNA under the control of the methanol-inducible alcohol oxidase promoter. The cDNA was cloned from in vitro amplified cDNA of **rabbit** liver mRNA. The nucleotide sequence of the cloned cDNA differed slightly from the previously published sequence that changed the amino acid sequence in six residues. Interestingly, five of these replacements are identical to the corresponding residues in human CEPT. In addition, the encoded mature N-terminal sequence was changed from Cys- to Arg-Glu-Phe- to link the **CETP** sequence to the yeast acid phosphatase signal peptide. The culture medium of the transformed cells induced with 1% methanol contained both cholesteryl ester and triglyceride transfer activity comparable to that of **rabbit** plasma. Like **rabbit** plasma, the lipid transfer activity in the medium could be inhibited by monoclonal antibodies that block CE/TG transfer or TG transfer alone. Immunoblot analysis of M(r) = 80 K and minor species of M(r) = 60-100 K. In spite of these differences, the specific transfer activity of the **recombinant CETP** was indistinguishable from that of **rabbit** plasma **CETP** of M(r) = 74 K. N-Glycosidase F treatment converted both the **recombinant** and plasma **CETP** to a single species of M(r) = 55 K. Both the plasma and **recombinant CETP** lost their activity after removal of

N-linked carbohydrate and sialic acid. A single 55 K component was found in the cell-lysates. The intracellular form of the **recombinant CETP** was not modified by N-glycosidase F treatment. In conclusion, the **recombinant CETP** is synthesized as an inactive polypeptide that is processed and secreted as a functional glycoprotein. In addition, the N-terminal Cys residue of the plasma **CETP** is not required for its activity.

L8 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 2002 ISI (R)
96:725538 The Genuine Article (R) Number: VK398. PLASMA PHOSPHOLIPID MASS-TRANSFER RATE - RELATIONSHIP TO PLASMA PHOSPHOLIPID AND CHOLESTERYL ESTER TRANSFER ACTIVITIES AND LIPID PARAMETERS. CHEUNG M C; WOLFBAUER G; ALBERS J J (Reprint). WASHINGTON UNIV, SCH MED, DEPT MED, NW LIPID RES LAB, 2121 N 35TH ST, SEATTLE, WA, 98103 (Reprint); WASHINGTON UNIV, SCH MED, DEPT MED, NW LIPID RES LAB, SEATTLE, WA, 98103. BIOCHIMICA ET BIOPHYSICA ACTA-LIPIDS AND LIPID METABOLISM (27 SEP 1996) Vol. 1303, No. 2, pp. 103-110. ISSN: 0005-2760. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human plasma phospholipid transfer protein (PLTP) has been shown to facilitate the transfer of phospholipid from liposomes or isolated very low and low density lipoproteins to high density lipoproteins. Its activity in plasma and its physiological function are presently unknown. To elucidate the role of PLTP in lipoprotein metabolism and to delineate factors that may affect the rate of phospholipid transfer between lipoproteins, we determined the plasma phospholipid mass transfer rate (PLTR) in 16 healthy adult volunteers and assessed its relationship to plasma lipid levels, and to phospholipid transfer activity (PLTA) and cholesteryl ester transfer activity (CETA) measured by radioassays. The plasma PLTR in these subjects was 27.2 +/- 11.8 nmol/ml per h at 37 degrees C (mean +/- S.D.), and their PLTA and CETA were 13.0 +/- 1.7 mu mol/ml per h and 72.8 +/- 15.7 nmol/ml per h, respectively. Plasma PLTR was correlated directly with total, non-HDL, and HDL triglyceride (r(s) = 0.76, P < 0.001), total and non-HDL phospholipid (r(s), > 0.53, P < 0.05), and inversely with HDL free cholesterol (r(s) = -0.54, P < 0.05), but not with plasma PLTA and CETA. When 85% to 96% of the PLTA in plasma was removed by polyclonal antibodies against **recombinant** human PLTP-phospholipid mass transfer from VLDL and LDL to HDL was reduced by 50% to 72%, but 80% to 100% of CETA could still be detected. These studies demonstrate that PLTP plays a major role in facilitating the transfer of phospholipid between lipoproteins, and suggest that triglyceride is a significant modulator of intravascular phospholipid transport. Furthermore, most of the PLTP and **CETP** in human plasma is associated with different particles. Plasma PLTA and CETA were also measured in mouse, rat, hamster, guinea pig, **rabbit**, dog, pig, and monkey. Compared to human, PLTA in rat and mouse was significantly higher and in **rabbit** and guinea pig was significantly lower while the remaining animal species had PLTA similar to humans. No correlation between PLTA and CETA was observed among animal species.

L8 ANSWER 7 OF 7 MEDLINE DUPLICATE 4
94045262 Document Number: 94045262. PubMed ID: 8228645. Use of fluorescent cholesteryl ester microemulsions in **cholesteryl ester transfer protein** assays. Bisgaier C L; Minton L L; Essenburg A D; White A; Homan R. (Department of Pharmacology, Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI 48105.) JOURNAL OF LIPID RESEARCH, (1993 Sep) 34 (9) 1625-34. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB In the present report we describe a simple and practical method to assess **CETP** activity in a defined system by use of microemulsions containing a fluorescent cholesteryl ester analog. The microemulsions are stable, simple to prepare, and can be made to defined composition. Initial

transfer rates are easily determined by monitoring changes in fluorescence. We have used the fluorescent cholesteryl ester analog, cholesteryl 4,4-difluoro-5,7-dimethyl-4-boro-3 alpha, 4 alpha-diaza-3-indacenedodecanoate (BODIPY-CE), to demonstrate the utility of this assay. The assay takes advantage of the concentration-dependent self-quenching of BODIPY-CE, when this analog is incorporated into microemulsions. We have used this new assay to demonstrate fluorescent lipid transfer facilitated by **rabbit** and human d > 1.21 g/ml plasma fraction and **recombinant** human **CETP**. A known inhibitory monoclonal antibody (Mab) to human **CETP** blocked BODIPY-CE transfer in a dose-dependent manner. We have also used BODIPY-CE microemulsions to measure **CETP** activity in whole plasma.

```
=> s l3 and simian

L9            0 L3 AND SIMIAN

=> d his


     (FILE 'HOME' ENTERED AT 10:54:09 ON 15 JAN 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:54:28 ON
     15 JAN 2002
L1          3632 S CETP
L2          2942 S L1 AND CHOLESTERYL ESTER TRANSFER PROTEIN
L3           107 S L2 AND RECOMBINANT
L4            90 S L3 AND HUMAN
L5             2 S L4 AND VACCINE
L6             2 DUP REMOVE L5 (0 DUPLICATES REMOVED)
L7            23 S L3 AND RABBIT
L8             7 DUP REMOVE L7 (16 DUPLICATES REMOVED)
L9             0 S L3 AND SIMIAN

=> s l2 and rabbit

L10         271 L2 AND RABBIT

=> s l10 and treatment

L11          47 L10 AND TREATMENT

=> dup remove l11

PROCESSING COMPLETED FOR L11
L12           25 DUP REMOVE L11 (22 DUPLICATES REMOVED)

=> d l12 1-25 cbib abs


L12  ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2002 ACS
2001:651566   Document No. 135:225853  Plasmid-based vaccine for treating
     atherosclerosis.  Thomas, Lawrence J. (AVANT Immunotherapeutics, Inc.,
     USA).  U.S. US 6284533 B1 20010904, 35 pp., Cont.-in-part of U.S. Ser.
No.
     802,967.  (English).  CODEN: USXXAM.  APPLICATION: US 1998-171969
     19981002.  PRIORITY: US 1996-PV52983 19960501; US 1997-802967 19970221;
WO
     1997-US7294 19970501.
AB   A plasmid-based vaccine is provided herein based on the combination of
DNA
     segments coding for one or more B cell epitopes of cholesteryl
```

ester transfer protein (**CETP**) and
one or more broad range helper T cell epitopes. Administration of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or **treatment** of atherosclerosis.

L12 ANSWER 2 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:563015 The Genuine Article (R) Number: 451VP. **Cholesteryl ester transfer protein** biosynthesis and
cellular cholesterol homeostasis are tightly interconnected. Izem L; Morton R E (Reprint). Cleveland Clin Fdn, Dept Cell Biol, Lerner Res Inst,
9500 Euclid Ave, NC10, Cleveland, OH 44195 USA (Reprint); Cleveland Clin Fdn, Dept Cell Biol, Lerner Res Inst, Cleveland, OH 44195 USA. JOURNAL OF BIOLOGICAL CHEMISTRY (13 JUL 2001) Vol. 276, No. 28, pp. 26534-26541. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0021-9258. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Cholesteryl ester transfer protein** (**CETP**) mediates triglyceride and cholesteryl eater (CE) transfer between lipoproteins, and its activity is strongly modulated by dietary cholesterol. To better understand the regulation of **CETP** synthesis and the relationship between **CETP** levels and cellular lipid metabolism, we selected the SW872 adipocytic cell line as a model. These cells secrete **CETP** in a time-dependent manner at levels exceeding those observed for Caco-2 or HepG2 cells. The addition of LDL, 25OH-cholesterol, oleic acid, or acetylated LDL to SW872 cells increased **CETP** secretion (activity and mass) up to 6-fold. In contrast, **CETP** production was decreased by almost 60% after **treatment** with lipoprotein-deficient serum or P-cyclodextrin, These effects, which were paralleled by changes in **CETP** mRNA, show that **CETP** biosynthesis in SW872 cells directly correlates with cellular lipid status. To investigate a possible, reciprocal relationship between **CETP** expression and cellular lipid homeostasis, **CETP** biosynthesis in SW872 cells was suppressed with **CETP** antisense oligonucleotides. Antisense oligonucleotides reduced **CETP** secretion (activity and mass) by 60% compared with sense-treated cells. When **CETP** synthesis was suppressed for 24 h, triglyceride synthesis was unchanged, but cholesterol biosynthesis was reduced by 20%, and acetate incorporation into CE increased 31%, After 3 days of suppressed **CETP** synthesis, acetate incorporation into the CE pool increased 3-fold over control. This mirrored a similar increase in CE mass. The efflux of free cholesterol to HDL was the same in sense and antisense-treated cells; however, HDL-induced CE hydrolysis in antisense-treated cells was diminished a-fold even though neutral CE hydrolase activity was unchanged. Thus, **CETP**-compromised SW872 cells display a phenotype characterized by inefficient mobilization of CE stores leading to CE accumulation. These results strongly suggest that **CETP** expression levels contribute to normal cholesterol homeostasis in adipocytic cells. Overall, these studies demonstrate that lipid homeostasis and **CETP** expression are tightly coupled.

L12 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2002 BIOSIS
2001:298985 Document No.: PREV200100298985. An extended toxicologic evaluation
of an immunoneutralizing vaccine to produce anti-**CETP** antibodies for the prevention/**treatment** of atherosclerosis. Thomas, Lawrence J. (1); Picard, Michele D. (1); Miller, David P. (1); Emmett, Constance D. (1); Scesney, Susanne M. (1); Pisano, Milissa L. (1); Adari,

Hedy (1); Hammond, Russell A. (1); Marsh, Henry C. (1); Rittershaus, Charles W. (1); Pettey, Carolyn L. (1). (1) AVANT Immunotherapeutics, 119 Fourth Ave., Needham, MA, 02494 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A566. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB A toxicology study was conducted with an immunoneutralizing vaccine designed to elicit antibodies that would bind to and block the function of **cholesteryl ester transfer protein** (**CETP**), in order to prevent atherosclerosis. The vaccine consisted of a dimer of a 31 a.a. synthetic chimeric peptide containing an N-terminal cysteine, a T cell epitope (residues 830-843 of tetanus toxin), and a B cell epitope (residues 461-476 of human **CETP**), formulated with an alum adjuvant. In this study NZW **rabbits** were immunized with either 0 mg (4 males and 4 females), 0.1 mg (2 males and 2 females), 0.25 mg (4 males and 4 females) or 1.0 mg (4 males and 4 females) of the vaccine on days 1, 29 and 57. On day 197 (at a relative antibody minimum) half of the animals from groups 1, 3 and 4 were sacrificed. The remaining animals were reboosted and euthanized on day 211, at an expected antibody maximum. Blood samples were taken periodically throughout the study and were assessed for hematology, clinical chemistry, and antibody titers. All **rabbits** in the non-control groups developed anti-**rabbit CETP** antibody titers, thus validating the immunogenicity of the vaccine. In all other measurements the vaccinated groups were indistinguishable from the control group. All animals were monitored for clinical abnormalities throughout the study, and at necropsy, gross pathology was assessed, selected organs were weighed, and samples of 44 tissues were taken for histopathology. By all the above parameters, no significant test article-related pathology was observed. This study demonstrated the administration of this **CETP** immunoneutralizing vaccine produced specific self-reactive antibody titers but no detectable test article-related pathology.

L12 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2002 ACS

2002:4125 An immunotherapeutic approach for the **treatment** of low plasma HDL-Cholesterol. Ryan, Una S.; Rittershaus, Charles W. (AVANT Immunotherapeutics, Inc., Needham, MA, 02494-2725, USA). NATO Science Series, Series I: Life and Behavioural Sciences, 330(Vascular Endothelium), 26-33 (English) 2001. CODEN: NSSSC9. ISSN: 1566-7693. Publisher: IOS Press.

AB One determinant of plasma HDL-Cholesterol concn. is **cholesteryl ester transfer protein** (**CETP**) activity. Inhibition of **CETP** activity increases plasma HDL-C, thus providing a potential therapeutic target for the **treatment** of atherosclerosis. Using a vaccine approach, we immunized New Zealand White **rabbits** with a peptide contg. a region of **CETP** known to be required for neutral lipid transfer function. **CETP** -vaccinated **rabbits** had significantly reduced plasma **CETP** activity and an altered lipoprotein profile compared with control **rabbits**. In a cholesterol-fed **rabbit** model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher, and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group compared with the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated **rabbits** compared with controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP**, and support the concept that inhibition of **CETP** activity in vivo can be anti-atherogenic. Currently, this

vaccine is in clin. trials.

L12 ANSWER 5 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000326614 EMBASE Antiatherogenic effect of the extract of Allium victorialis
on the experimental atherosclerosis in the **rabbit** and transgenic mouse. Tae Gyn Kim; Seung Hee Kim; Soeg Youn Kang; Ki Kyung Jung; Don Ha Choi; Yong Bok Park; Jong Hoon Ryu; Hyung Mee Han. H.M. Han, Natl. Inst. of Toxicological Res., Korea Food and Drug Administration, Seoul 122-704, Korea, Republic of. Korean Journal of Pharmacognosy 31/2 (149-156) 2000.
Refs: 25.
ISSN: 0253-3073. CODEN: SYHJAM. Pub. Country: Korea, Republic of.
Language: Korean. Summary Language: English.
AB Atherosclerosis is emerging as one of the major causes of death in Korea as well as Western societies. In the present study, hypocholesterolemic and antiatherogenic effects of the ethanol extract of Allium victorialis Makino was investigated using the conventional **rabbit** and the **cholesteryl ester transfer protein** (**CETP**)-transgenic mouse model. Hypercholesterolemia was induced by feeding high cholesterol diet to the animals for 30 days and they were then fed with high cholesterol diet containing 0.5% of the A. victorialis extract for additional 30 (or 40) days. In the experiment using **rabbits**, **treatment** with the A. victorialis extract significantly decreased plasma total cholesterol, low density lipoprotein (LDL)-cholesterol, triglyceride levels and lipid peroxidation compared to those in the control group. Total cholesterol contents in the liver and the heart were also significantly decreased. Lipid staining of the aorta isolated from the **rabbits** showed that **treatment** with the A. victorialis extract decreased formation of atheromatous plaques on the intima of the aorta. In the experiment employing **CETP** transgenic mouse model, **treatment** with the A. victorialis extract decreased the levels of plasma total cholesterol and the tissue triglyceride levels in the heart. These results demonstrated that the ethanol extract of A. victorialis lowered serum cholesterol levels, tissue lipid contents and accumulation of cholesterol in the artery.

L12 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2002 ACS
1999:282118 Document No. 130:310673 Xenogeneic **cholesteryl ester transfer protein** (**CETP**) for modulation of **CETP** activity in **treatment** of atherosclerosis. Rittershaus, Charles W.; Thomas, Lawrence J. (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.
AB Methods for modulating **cholesteryl ester transfer protein** (**CETP**) activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based vaccine for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

L12 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2002 ACS
1999:223038 Document No. 130:250711 Vector vaccines against cholesterol

ester transfer protein for the **treatment** of atherosclerosis. Needleman, Philip; Glenn, Kevin (Monsanto Company, USA). PCT Int. Appl. WO 9915655 A1 19990401, 99 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19366 19980917. PRIORITY: US 1997-934367 19970919.

AB Expression vectors for manuf. of antigenic fragments of **cholesteryl ester transfer protein** (**CETP**) that can be used to inactivate the protein are described. The protein plays a key role in the transfer of cholesterol from HDL to LDL and VLDL and inhibition of **CETP** synthesis can be used to prevent LDL and VLDL formation in the prophylaxis of atherosclerosis. Immunogens, inocula, DNA segments, and recombinant DNA mol. vectors useful for carrying out the invention are also disclosed. The use of antigenic fragments of **rabbit CETP** to raise autoantibodies in **rabbits** is demonstrated. Antibodies to three such peptides cross-reacted with human **CETP**. **Rabbits** vaccinated with these antigens showed a .apprx.10% increase in serum HDL. Antigens were manufd. as fusion proteins with hepatitis B core antigens in Escherichia coli, in a baculovirus system, and in mammalian cell culture.

L12 ANSWER 8 OF 25 BIOSIS COPYRIGHT 2002 BIOSIS

1999:282999 Document No.: PREV199900282999. A vaccine to produce anti-**cholesteryl ester transfer protein** (**CETP**) antibodies for the prevention/**treatment** of atherosclerosis. Thomas, L. J. (1); Picard, M. D. (1); Miller, D. P. (1); Honan, C. M. (1); Adari, H. (1); Emmett, C. D. (1); Marsh, H. C. (1); Ryan, U. S. (1); Pettey, C. L. (1); Rittershaus, C. W. (1). (1) Avant Immunotherapeutics, Inc., Needham, MA, 02494 USA. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A693. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April 17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L12 ANSWER 9 OF 25 MEDLINE DUPLICATE 1

1999333246 Document Number: 99333246. PubMed ID: 10406588. Combined effects of probucol and benzafibrate on lipoprotein metabolism and liver **cholesteryl ester transfer protein** mRNA in cholesterol-fed **rabbits**. Ou J; Saku K; Jimi S; Liao Y L; Ohta T; Zhang B; Arakawa K. (Department of Internal Medicine, Fukuoka University School of Medicine, Japan.) JAPANESE CIRCULATION JOURNAL, (1999 Jun) 63 (6) 471-7. Journal code: KGN; 7806868. ISSN: 0047-1828. Pub. country: Australia. Language: English.

AB Probucol decreases and bezafibrate increases plasma high density lipoprotein-cholesterol (HDL-C) levels in humans. This study was performed to determine whether the HDL-C-lowering effects of probucol could be reversed by **treatment** with bezafibrate in hypercholesterolemic **rabbits**. Forty-nine normolipidemic Japanese White **rabbits** were divided into 5 groups [group 1: normal chow; group 2: 0.2% cholesterol (Ch) diet; group 3: 0.2% Ch and 1% probucol diet; group 4: 0.2% Ch and 1% bezafibrate diet; group 5: 0.2% Ch and 1% probucol plus 1% bezafibrate diet] and treated for 8 weeks. Plasma lipids, **cholesteryl ester transfer protein** (**CETP**) activity in the lipoprotein-deficient plasma fraction, **CETP** mRNA in liver tissue and plasma drug concentrations were investigated. Serum total cholesterol (TC) increased after the

rabbits in groups 2, 3, 4 and 5 were fed Ch, but overall, no significant differences were observed in serum TC and triglyceride (TG) among these groups. Serum HDL-C levels increased ($p<0.01$) in the bezafibrate-treated group, but a significant ($p<0.05$) reduction in HDL-C was observed in both the Ch + probucol (group 3) and Ch + probucol plus bezafibrate (group 5) groups; no significant difference was observed between groups 3 and 5. Significant correlation ($p<0.01$) was found between serum low density lipoprotein cholesterol (LDL-C) levels and plasma probucol concentrations in groups 3 and 5, but no correlation was found between plasma concentrations of probucol/bezafibrate and serum HDL-C levels. **CETP** activity in the lipoprotein-deficient plasma fraction increased in the Ch-, Ch + probucol-, and Ch + probucol and bezafibrate-fed groups (groups 2, 3 and 5, respectively), whereas a significant reduction in this activity was observed in the Ch + bezafibrate-fed group (group 4). An analysis of covariance showed that the **CETP** activity responded more sensitively to drug **treatment** than did the serum HDL-C level. **CETP** mRNA in liver tissue was assessed by Northern blotting at 8 weeks, but no changes were observed among the 5 groups. Probucol decreased and bezafibrate increased serum HDL-C levels, through **CETP** activity without affecting liver **CETP** mRNA levels, and the decrease in HDL-C levels produced by probucol could not be reversed by bezafibrate.

L12 ANSWER 10 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)

1999:60305 The Genuine Article (R) Number: 154VW. The hepatic uptake of rat high-density lipoprotein cholesteryl ester is delayed after **treatment** with **cholesteryl ester transfer protein**. Botham K M; Avella M; Cantafora A; Bravo E (Reprint). IST SUPER SANITA, LAB METAB & BIOCHIM PATOL, VIALE REGINA ELENA 299, I-00161 ROME, ITALY (Reprint); IST SUPER SANITA, LAB METAB & BIOCHIM PATOL, I-00161 ROME, ITALY; UNIV LONDON ROYAL VET COLL, DEPT VET BASIC SCI, LONDON NW1 0TU, ENGLAND. PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE (JAN 1999) Vol. 220, No. 1, pp. 31-38. Publisher: BLACKWELL SCIENCE INC. 350 MAIN ST, MALDEN, MA 02148. ISSN: 0037-9727. Pub. country: ITALY; ENGLAND. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The effects of **cholesteryl ester transfer protein** (**CETP**) on the direct uptake of HDL cholesteryl ester by the liver was investigated using the rat in vivo and the isolated perfused rat liver as experimental models, Rat plasma was incubated with [H-3]cholesterol in the presence or absence of partially purified human **CETP** far 18 hr and [H-3]cholesteryl ester-labeled HDL was then isolated by ultracentrifugation, The **CETP**-treated as compared to untreated HDL showed a small shift toward a lower density in the peak of lipoprotein cholesterol, suggesting that the HDL particle size was increased, After injection of the labeled HDL into rats in vivo, more radioactivity remained in the plasma after 60 min when the **CETP** -treated preparation was used, but the amounts found in the liver and secreted in the bile were not significantly different from those obtained with the untreated HDL, The distribution of the label remaining in the plasma after 60 min between different density fractions corresponding to HDL subclasses suggested that the uptake of HDL, and HDL, was delayed by **CETP treatment**. Radioactivity from **CETP** -treated HDL was also removed from the perfusate of isolated perfused rat livers more slowly than that from untreated HDL, and in this case the amount found in the liver after 60 min was significantly lower, These findings indicate that **treatment** with **CETP** has a direct inhibitory effect on the clearance of rat HDL cholesteryl ester from the blood and its uptake by the liver.

L12 ANSWER 11 OF 25 MEDLINE DUPLICATE 2

1998328362 Document Number: 98328362. PubMed ID: 9665425. Human **cholesteryl ester transfer protein** measured by enzyme-linked immunosorbent assay with two monoclonal antibodies against **rabbit cholesteryl ester transfer protein**: plasma **cholesteryl ester transfer protein** and lipoproteins among Japanese hypercholesterolemic patients. Sasai K; Okumura-Noji K; Hibino T;
Ikeuchi R; Sakuma N; Fujinami T; Yokoyama S. (Department of Biochemistry I, Nagoya City University Medical School, Nagoya, Japan.) CLINICAL CHEMISTRY, (1998 Jul) 44 (7) 1466-73. Journal code: DBZ; 9421549. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB Plasma **cholesteryl ester transfer protein** (**CETP**) concentrations were measured in Japanese subjects by an ELISA with two different monoclonal antibodies that were raised against **rabbit CETP** and cross-reacted against human **CETP**. Among 63 patients who consecutively underwent coronary angiography, the plasma **CETP** of 37 patients with luminal stenosis > or = 50% in their coronary arteries was not significantly different from that of the 26 patients with luminal stenosis
< 50%. No other lipoprotein-related measurement except HDL-cholesterol differentiated the two groups. Among 40 hypercholesterolemic patients, no lipoprotein-related measurement other than LDL-cholesterol was found to positive correlate with the **CETP**. Before and after the **treatment** of 23 patients with simvastatin 5 mg a day for 4 weeks, plasma **CETP** markedly decreased in those whose pretreatment **CETP** was > or = 3 mg/L; no change was observed for those with lower pretreatment **CETP**. In the former group, negative correlation between **CETP** and HDL-cholesterol was demonstrated only in the posttreatment plasma.

L12 ANSWER 12 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:714948 The Genuine Article (R) Number: 119MA. Role of female sex steroids in regulating **cholesteryl ester transfer protein** in transgenic mice. Vadlamudi S; MacLean P; Green T; Shukla N; Bradfield J; Vore S; Barakat H (Reprint). E CAROLINA UNIV, SCH MED, DEPT BIOCHEM, GREENVILLE, NC 27858 (Reprint); E CAROLINA UNIV, SCH MED, DEPT BIOCHEM, GREENVILLE, NC 27858; E CAROLINA UNIV, SCH MED, DEPT COMPARAT MED, GREENVILLE, NC 27858.
METABOLISM-CLINICA
L AND EXPERIMENTAL (SEP 1998) Vol. 47, No. 9, pp. 1048-1051. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0026-0495. Pub. country: USA.
Language:
English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The role of sex steroids in the regulation of **cholesteryl ester transfer protein** (**CETP**) was examined in the following groups of female transgenic mice carrying the human **CETP** gene: (1) normal, (2) ovariectomized, (3) ovariectomized and treated with estrogen; (4) ovariectomized and treated with progesterone; (5) ovariectomized and treated with both hormones, and (6) ovariectomized and treated with tamoxifen. **CETP** activity was measured in the plasma, and in the particulate and the soluble fractions of liver, muscle, and adipose tissue, Human **CETP** specific activity was determined by taking the difference of cholesterol ester transfer in the presence and absence of an antibody (TP2) against human **CETP**. Ovariectomy reduced hormone levels, but did not completely abolish them from the circulation. Plasma **CETP** activity was significantly reduced in the tamoxifen group. There were significant reductions in **CETP** in liver homogenate and the soluble fraction, as well as in the particulate fraction of adipose with ovariectomy. Hormone replacement did not restore **CETP** activity in either the

plasma or the tissues, Tamoxifin **treatment** resulted in a decrease in **CETP** activity in both fractions of liver, but had no effect on adipose. In the soluble fraction of adipose tissue and both fractions of muscle, only trace **CETP** activity was detected. We conclude that (1) minimal amounts of sex steroid hormones may be sufficient to affect **CETP** expression; (2) the effects of sex steroid hormones vary among tissues; and (3) in addition to the sex steroids, factor(s) from the ovary are needed for the full expression of **CETP** in this animal model. Copyright (C) 1998 by W.B. Saunders Company.

L12 ANSWER 13 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:652632 The Genuine Article (R) Number: 112MJ. Mechanism of action of probucol on **cholesteryl ester transfer protein** (**CETP**) mRNA in a Chinese hamster ovary cell line that had been stably transfected with a human **CETP** gene. Ou J F; Saku K (Reprint); Jimi S; Ohta T; Zhang B; Pownall H J; Shimada Y; Tsujita Y; Arakawa K. FUKUOKA UNIV, SCH MED, DEPT INTERNAL MED, 45-1-7 NANKUMA JONANKU, FUKUOKA 81480, JAPAN (Reprint); FUKUOKA UNIV, SCH MED, DEPT INTERNAL MED, FUKUOKA 81480, JAPAN; FUKUOKA UNIV, SCH MED, DEPT PATHOL, FUKUOKA 81480, JAPAN; UNIV RYUKYUS, SCH MED, DEPT PEDIAT, OKINAWA 90301, JAPAN; BAYLOR COLL MED, DEPT INTERNAL MED, HOUSTON, TX 77030; SANKYO CO LTD, PHARMACOL & MOL BIOL RES LABS, TOKYO 140, JAPAN.

BIOCHIMICA ET BIOPHYSICA ACTA-LIPIDS AND LIPID METABOLISM (31 JUL 1998) Vol. 1393, No. 1, pp. 153-160. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0005-2760. Pub. country: JAPAN; USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Probucol, a widely used lipid-lowering agent, is associated with a significant reduction of plasma high density lipoprotein (HDL)-cholesterol levels. To examine the mechanism of probucol HDL-lowering and probucol's effects on **cholesteryl ester transfer protein** (**CETP**) and cholesterol metabolism in cells, we used a Chinese hamster ovary (CHO) cell line that had been stably transfected with a human **CETP** gene (hCETP-CHO). After this cell line was incubated with various concentrations of probucol (5, 10 and 50 mu M) for 24 h, mean intracellular probucol concentrations reached 0.47, 0.67, and 1.52 mu g/mg cell protein, respectively. Northern blot analysis showed that cellular **CETP** mRNA was increased by probucol in a dose-dependent manner (137%, 162%, and 221% of the control, respectively).

The specific CET activity in the culture medium, measured as the percentage of [H-3]cholesterol oleate transferred from discoidal bilayer particles (which mimic HDL) to LDL, also increased in a dose-dependent manner. Intracellular total cholesterol levels were decreased to 87.5%, 74.9%, and 52.5% of the control, respectively. Probucol had no effects on HMG-CoA reductase activity or cholesterol synthesis from [1-C-14]acetate in hCETP-CHO. However, C-14-incorporated cholesterol secretion into the culture medium from hCETP-CHO was increased to 181%, 256% and 354% of the control by 5, 10 and 50 mu M probucol, respectively. We concluded that (1) **treatment** with probucol increased the **CETP** mRNA level and specific CET activity in the hCETP-CHO cell line, and (2) probucol promoted cholesterol efflux from hCETP-CHO, which resulted in a decrease in intracellular cholesterol levels. (C) 1998 Elsevier Science B.V. All rights reserved.

L12 ANSWER 14 OF 25 MEDLINE DUPLICATE 3

1998270051 Document Number: 98270051. PubMed ID: 9607128. Lowering of serum **cholesteryl ester transfer protein**--but not lecithin:cholesterol acyltransferase--activity levels by hypocholesterolemic drugs in the **rabbit**. Meijer G W;

Groener J E; Beynen A C; Van Tol A. (Department of Laboratory Animal Science, University of Utrecht, The Netherlands.. Gert.Meijer@unilever.com) . CARDIOVASCULAR DRUGS AND THERAPY, (1998 Mar) 12 (1) 13-8. Journal code: AYG; 8712220. ISSN: 0920-3206. Pub. country: United States. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) and lecithin:cholesterol acyltransferase (LCAT) are important factors in the regulation of serum lipoprotein metabolism. **Rabbits** were fed hypocholesterolemic drugs to investigate the effect on serum **CETP** and LCAT activity levels. The activities were assayed using exogenous substrate assays and are an estimate of **CETP** and LCAT mass. Groups of eight **rabbits** were fed a cholesterol-free diet containing either 0.03% simvastatin or 1% cholestyramine for 6 weeks. For comparison eight **rabbits** were fed a cholesterol-free control diet without drugs or a diet containing 0.1% cholesterol for 6 weeks. Total serum and lipoprotein triglyceride concentrations were not different after intervention with the hypocholesterolemic drugs or the cholesterol diet. Dietary cholesterol induced higher VLDL, IDL, and LDL cholesterol, as well as serum **CETP** activity, as expected. Serum LCAT activity showed little change with intervention. Both simvastatin and cholestyramine tended to lead to decreased cholesterol in all lipoprotein fractions and caused a significant decrease in serum **CETP** activity when compared with the control diet. Both drugs also caused a significant lower LDL particle concentration, as judged from differences in LDL protein levels. Intervention with simvastatin or cholestyramine led to relatively cholesterol-poor LDL. These effects on LDL concentration and composition were opposite from the effects of cholesterol feeding. Differences in the cholesterol contents of VLDL and IDL were comparable with those in LDL. The results suggest that decreasing serum **CETP** activity levels by **treatment** with simvastatin or cholestyramine may contribute to lowering of cholesterol apo B-containing lipoproteins. The effects are additional to the well-known increase in hepatic LDL receptor activity, which is likely to be the most important factor in LDL cholesterol lowering by these drugs.

L12 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2002 ACS

1997:736947 Document No. 128:20966 Large versus small unilamellar vesicles mediate reverse cholesterol transport in vivo into two distinct hepatic metabolic pools: implications for the **treatment** of atherosclerosis. Rodrigueza, Wendi V.; Mazany, Kirstin D.; Essenburg, Arnold D.; Pape, Michael E.; Rea, Thomas J.; Bisgaier, Charles L.; Williams, Kevin Jon (Dep. Biochem., Med. Coll. Pennsylvania, Philadelphia, PA, USA). Arterioscler., Thromb., Vasc. Biol., 17(10), 2132-2139 (English) 1997. CODEN: ATVBFA. ISSN: 1079-5642. Publisher: American Heart Association.

AB Phospholipid liposomes are synthetic mediators of "reverse" cholesterol transport from peripheral tissue to liver in vivo and can shrink atherosclerotic lesions in animals. Hepatic disposal of this cholesterol, however, has not been examd. We compared hepatic effects of large (.apprxeq.120-nm) and small (.apprxeq.35-nm) unilamellar vesicles (LUVs and SUVs), both of which mediate reverse cholesterol transport in vivo but were previously shown to be targeted to different cell types within the liver. On days 1, 3, and 5, **rabbits** were i.v. injected with 300 mg phosphatidylcholine (LUVs or SUVs) per kg body wt. or with the equiv. vol. of saline. After each injection, LUV- and SUV-injected animals showed large increases in plasma concns. of unesterified cholesterol, indicating mobilization of tissue stores. After hepatic uptake of this cholesterol, however, SUV-treated animals developed persistently elevated plasma LDL concns.,which by day 6 had increased to more than four times the values in saline-treated controls. In contrast, LUV-treated animals

showed normal LDL levels. By RNase protection assay, SUVs suppressed hepatic LDL receptor mRNA at day 6 (to 61.+-.4% of control, mean.+-.SEM), whereas LUVs caused a statistically insignificant stimulation. Hepatic HMG-CoA reductase message was also significantly suppressed with SUV, but not LUV **treatment**, and hepatic 7.alpha.-hydroxylase message showed a similar trend. These data on hepatic mRNA levels indicate that SUVs, but not LUVs, substantially perturbed liver cholesterol homeostasis.

We conclude that LUVs and SUVs mobilize peripheral tissue cholesterol and deliver it to the liver, but to distinct metabolic pools that exert different regulatory effects. The effects of one of these artificial particles, SUVs, suggest that reverse cholesterol transport may not always be benign. In contrast, LUVs may be a suitable therapeutic agent, because they mobilize peripheral cholesterol to the liver without suppressing hepatic LDL receptor mRNA with without provoking a subsequent rise in plasma LDL levels.

L12 ANSWER 16 OF 25 MEDLINE DUPLICATE 4
97442869 Document Number: 97442869. PubMed ID: 9297800. Lack of effect of vitamin E on cholesteryl ester transfer and lipoprotein composition in cholesterol-fed **rabbits**. Liu X Q; Buchanan W; Matthews A J; Chung B H; Bagdade J D. (Department of Medicine, Rush Medical College, Chicago, IL 60612, USA.) COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY. PART B, BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1997 Aug) 117 (4) 553-9. Journal code: CF9; 9516061. ISSN: 1096-4959. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The concentration and activity of **cholesteryl ester transfer protein** (**CETP**) is increased in plasma in hypercholesterolemic humans and in experimental animals fed cholesterol. While the concentration of lipo-proteins appears to be the major determinant of **CETP** activity, we have found previously that dietary measures and pharmacologic agents that alter their lipid composition reduce the activity of **CETP** in plasma (CET). Since vitamin E is lipophilic and is incorporated into lipoproteins, we have examined the question of whether it too attenuates CET in cholesterol-fed New Zealand White **rabbits** prior to and 14 weeks after **treatment** with differing doses (5, 15, 30, 45 mg/kg) of vitamin E. Plasma triglycerides (TG), cholesterol (TC) and phospholipids (Lys, Sph, Lec, PI, PE) all increased significantly to a comparable degree in the **rabbits** fed cholesterol compared to those fed chow ($p < 0.05$; $p < 0.01$); the levels achieved were similar in the vitamin E-treated and untreated groups. As was observed with plasma lipids, cholesteryl ester transfer (CET) was accelerated to the same degree in each of the cholesterol-fed groups independent of whether they received vitamin E compared to chow-fed controls ($p < 0.01$) and the distribution of cholesterol in apo-B containing lipoproteins (VLDL, IDL, and LDL) was similar in the vitamin E-treated and untreated groups. These findings indicate that vitamin E has no discernible effect on CET when cholesterol levels are markedly elevated.

L12 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2002 BIOSIS
1997:144273 Document No.: PREV199799443476. A plasmid-based vaccine to elicit autoantibodies to **cholesteryl ester transfer protein** (**CETP**) for the prevention/**treatment** of atherosclerosis. Thomas, L. J.; Picard, M. D.; Stewart, S. E.; Waite, B. C. D.; Lin, A. Y.; Rittershaus, C. W.; Pettey, C. L.. T Cell Sci. Inc., Needham, MA USA. Journal of Allergy and Clinical Immunology, (1997) Vol. 99, No. 1 PART 2, pp. S187. Meeting Info.: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco,

California, USA February 21-26, 1997 ISSN: 0091-6749. Language: English.

L12 ANSWER 18 OF 25 MEDLINE DUPLICATE 5
96292476 Document Number: 96292476. PubMed ID: 8728322. Expression and secretion of **rabbit** plasma **cholesteryl ester transfer protein** by Pichia pastoris. Kotake H; Li Q; Ohnishi T; Ko K W; Agellon L B; Yokoyama S. (Lipid and Lipoprotein Research Group, University of Alberta, Edmonton, Canada.) JOURNAL OF LIPID RESEARCH, (1996 Mar) 37 (3) 599-605. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB The **rabbit cholesteryl ester transfer protein** (**CETP**) was expressed in the methylotrophic yeast Pichia pastoris by introducing the **CETP** cDNA under the control of the methanol-inducible alcohol oxidase promoter.

The cDNA was cloned from in vitro amplified cDNA of **rabbit** liver mRNA. The nucleotide sequence of the cloned cDNA differed slightly from the previously published sequence that changed the amino acid sequence in six residues. Interestingly, five of these replacements are identical to the corresponding residues in human CEPT. In addition, the encoded mature N-terminal sequence was changed from Cys- to Arg-Glu-Phe- to link the **CETP** sequence to the yeast acid phosphatase signal peptide. The culture medium of the transformed cells induced with 1% methanol contained both cholesteryl ester and triglyceride transfer activity comparable to that of **rabbit** plasma. Like **rabbit** plasma, the lipid transfer activity in the medium could be inhibited by monoclonal antibodies that block CE/TG transfer or TG transfer alone. Immunoblot analysis of M(r) = 80 K and minor species of M(r) = 60-100 K. In spite of these differences, the specific transfer activity of the recombinant **CETP** was indistinguishable from that of **rabbit** plasma **CETP** of M(r) = 74 K. N-Glycosidase F **treatment** converted both the recombinant and plasma **CETP** to a single species of M(r) = 55 K. Both the plasma and recombinant **CETP** lost their activity after removal of N-linked carbohydrate and sialic acid. A single 55 K component was found in the cell-lysates. The intracellular form of the recombinant **CETP** was not modified by N-glycosidase F **treatment**. In conclusion, the recombinant **CETP** is synthesized as an inactive polypeptide that is processed and secreted as a functional glycoprotein. In addition, the N-terminal Cys residue of the plasma **CETP** is not required for its activity.

L12 ANSWER 19 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
96:142093 The Genuine Article (R) Number: TV417. ETHANOL-INDUCED REDISTRIBUTION OF **CHOLESTERYL ESTER TRANSFER PROTEIN** (**CETP**) BETWEEN LIPOPROTEINS. HANNUKSELA M L; RANTALA M; KESANIEMI Y A; SAVOLAINEN M J (Reprint). UNIV OULU, DEPT INTERNAL MED, KAJAANINTIE 50, SF-90220 OULU, FINLAND (Reprint); UNIV OULU, DEPT INTERNAL MED, SF-90220 OULU, FINLAND; UNIV OULU, BIOCTR OULU, SF-90220 OULU, FINLAND. ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY (FEB 1996) Vol. 16, No. 2, pp. 213-221. ISSN: 1079-5642. Pub. country: FINLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Since alcohol drinking reduces the concentration and activity of plasma **cholesteryl ester transfer protein** (**CETP**), we investigated the effects of alcohol on its synthesis and secretion by perfusing **rabbit** livers for 4 hours in the absence or presence of ethanol. The quantity of **CETP** mRNA in the perfused livers did not differ between the control and ethanol (25 mmol/L or 50 mmol/L) perfusions. **CETP** activity was determined by incubating [H-3]cholesteryl ester-labeled human LDL and unlabeled human

HDL with the perfusion medium after removing the endogenous VLDL (secreted by the perfused liver) by ultracentrifugation. **CETP** activity in the perfusion medium increased at a linear rate that was not affected by ethanol. When the VLDL was removed by precipitation with polyethylene glycol or a heparin-Sepharose column instead of ultracentrifugation, practically no **CETP** activity was detected in the ethanol perfusions, whereas these procedures did not affect **CETP** activity in the control perfusions. Inhibition of ethanol oxidation by 4-methylpyrazole resulted in **CETP** activity similar to that of the controls. We conclude that ethanol does not affect the synthesis or secretion of **CETP**, but its oxidation may alter the distribution of **CETP** in lipoproteins. **CETP** seems to be present in VLDL as well as in HDL, and since VLDL is more rapidly catabolized than HDL, this may explain the low plasma **CETP** concentration associated with alcohol consumption.

L12 ANSWER 20 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
95:554334 The Genuine Article (R) Number: RN721. HIGH-DENSITY-LIPOPROTEIN AND APOLIPOPROTEIN-A-I DEFICIENCY INDUCED BY COMBINATION THERAPY WITH PROBUCOL AND BEZAFIBRATE. SAKU K (Reprint); ZHANG B; JIMI S; BAI H; HIRATA K; SASAKI N; LIU R; ARAKAWA K. FUKUOKA UNIV, SCH MED, DEPT INTERNAL MED, JONAN KU, 45-1-7 NANAKUMA, FUKUOKA 81401, JAPAN (Reprint). EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY (JUL 1995) Vol. 48, No. 3-4, pp. 209-215.
ISSN: 0031-6970. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The effects of the administration of slow-release bezafibrate to hypercholesterolaemic patients who were already receiving long-term probucol **treatment** (mean 865 days, 500-1000 mg . day(-1)) were investigated. Bezafibrate was administered at either 200 mg . day(-1) (13 males, 13 females, mean age 55.2 years) or 400 mg . day(-1) (11 males, 14 females, mean age 57.2 years), and blood was taken at 0, 3, 6 and 12 months after the beginning of combination therapy. Overall, serum total cholesterol (TC), triglyceride (TG), very low density lipoprotein (VLDL)-TC, high-density lipoprotein (HDL)-TG, VLDL-TG, VLDL-phospholipid (PL), lipoprotein (a) [Lp(a)], apolipoprotein (ape) C-III, apo E levels and LCAT activity decreased significantly with this combination therapy, while HDL cholesterol (C), HDL3-C, HDL-PL, apo A-I and apo A-II levels significantly increased, as assessed by analysis of variance (ANOVA). Five patients (one receiving 200 mg . day (-1), four receiving 400 mg . day(-1) bezafibrate) showed drastic reductions in HDL-C (HDL-C levels were reduced by a mean of 46.2%, 59.3% and 61.6% at 3, 6 and 12 months, respectively) after beginning combination therapy. These HDL-C reductions were maintained for the 1 year of combination therapy, but then returned to pre-combination **treatment** levels I month after discontinuation of bezafibrate. Serum probucol concentrations and **cholesteryl ester transfer protein** (**CETP**) mass were assayed at 6 months, and the probucol concentration was higher in the HDL-deficient group (56.2 vs 26.5 mu g/ml). In contrast, **CETP** mass was significantly lower in HDL-deficient patients than in non-HDL-deficient patients (2.08 vs 2.87 mg . l(-1)). When the patients in the non-HDL-deficient group were divided into two groups, receiving low(200 mg . day(-1), n = 25) and high (400 mg . day(-1) 21) doses of bezafibrate, the former group showed a significant increase in probucol-lowered HDL-C and apo A-I, although these levels did not return to pre-probucol **treatment** levels, while the latter group showed

no changes in HDL. These data suggest that the addition of a low dose of bezafibrate to probucol tended to reverse probucol-induced HDL lowering, while 9.8% (5 of 51 patients) of the patients exhibited a severe HDL deficiency. Since it is unclear whether or not such an extreme HDL reduction is harmful, HDL deficiency should be carefully monitored with this combination therapy.

L12 ANSWER 21 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
91:299081 The Genuine Article (R) Number: FM030. INCREASE IN PLASMA **CHOLESTERYL ESTER TRANSFER PROTEIN** DURING PROBUCOL **TREATMENT** - RELATION TO CHANGES IN HIGH-DENSITY-LIPOPROTEIN COMPOSITION. MCPHERSON R (Reprint); HOGUE M; MILNE R W; TALL A R; MARCEL Y L. MCGILL UNIV, ROYAL VICTORIA HOSP, LIPID RES LAB, H7 90, 687 PINE AVE W, MONTREAL H3A 1A1, QUEBEC, CANADA (Reprint); CLIN RES INST MONTREAL, LIPOPROT METAB LAB, MONTREAL H2W 1R7, QUEBEC, CANADA; COLUMBIA UNIV COLL PHYS & SURG, DEPT MED, NEW YORK, NY, 10032. ARTERIOSCLEROSIS AND THROMBOSIS (1991) Vol. 11, No. 3, pp. 476-481.
Pub. country: CANADA; USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Probucol is a hypolipidemic agent that causes a marked decrease in high density lipoprotein (HDL) cholesterol. To investigate the mechanism of this effect, two studies were performed in hypercholesterolemic patients who had been stabilized previously on diet and were not receiving other lipid-lowering medication. Plasma **cholesteryl ester transfer protein** (**CETP**) concentrations were measured in fasting plasma samples before and after 10 weeks of probucol therapy using a sensitive and specific radioimmunoassay. Plasma total and low density lipoprotein cholesterol concentrations decreased, whereas apolipoprotein (apo) B was unchanged. Plasma apo E concentrations increased markedly. HDL cholesterol and apo A-I decreased in all subjects. These effects of probucol were accompanied by even more striking changes in plasma **CETP** concentrations, which increased by a mean of 64%. In a second study of six hypercholesterolemic subjects, the time-course effects of probucol on **CETP** and HDL subspecies were studied. Significant increases in plasma apo E and in **CETP** occurred after 4 weeks, and **CETP**, but not apo E, increased further after 16 weeks of **treatment**. Concomitant and opposite changes occurred in HDL composition, with decreases in HDL cholesterol and lipoprotein containing apo A-I. The increase in plasma **CETP** concentrations, the decrease in HDL cholesterol, and the increase in plasma apo E concentrations observed during probucol **treatment** are changes consistent with a postulated increase in reverse cholesterol transport via the remnant pathway.

L12 ANSWER 22 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
91:177611 The Genuine Article (R) Number: FD249. CU2+-MEDIATED OXIDATION OF DIALYZED PLASMA - EFFECTS ON LOW AND HIGH-DENSITY-LIPOPROTEINS AND **CHOLESTERYL ESTER TRANSFER PROTEIN**.
ZAWADZKI Z; MILNE R W; MARCEL Y L (Reprint). CLIN RES INST MONTREAL, LIPOPROT MED LAB, 110 PINE AVE W, MONTREAL H2W 1R7, QUEBEC, CANADA. JOURNAL OF LIPID RESEARCH (1991) Vol. 32, No. 2, pp. 243-250. Pub. country: CANADA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We previously reported that the expression of an epitope of apolipoprotein B (apoB), mapped to the C-terminus and defined by antibody B(sol)7, increased during Cu2+-mediated oxidation of isolated low density lipoprotein (LDL). We describe now the properties of B(sol)7 as a marker of LDL oxidation in whole plasma in relation to other effects of oxidative

treatment of plasma, such as the distribution of apoA-I and **cholesteryl ester transfer protein** (CEPT). In dialyzed plasma, no LDL oxidation was detected at Cu2+ concentrations (5-mu-M) sufficient for extensive oxidation of isolated LDL. At a higher Cu2+ concentration (50-mu-M), an increased expression of the B(sol)7 epitope was observed; at 250-mu-M Cu2+, other evidence of LDL oxidation was found. The pattern of LDL response to Cu2+ observed in dialyzed plasma could be reproduced by adding 3% bovine serum albumin to isolated LDL. We demonstrate that the effect of albumin most likely results from its ability to bind copper ions. Incubation of plasma with increasing concentration of Cu2+ resulted first in the disappearance of alpha-2-migrating HDL, the usual carrier of **CETP**; free **CETP** and high molecular weight apoA-I-containing particles were also generated during oxidation. Addition of oxidized, but not native, LDL to plasma resulted in a transfer to LDL of some of the **CETP** initially associated with apoA-I.

In conclusion, the increased immunoreactivity of the B(sol)7 epitope was the most sensitive parameter of LDL oxidation, but other parameters, such as the presence of alpha-2-HDL and **CETP**-lipoprotein associations were even more sensitive evidence of lipoprotein oxidation.

L12 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2002 ACS

1989:450078 Document No. 111:50078 Enhanced cholesteryl ester transfer activity in cyclophosphamide-treated **rabbits**: relationship with lipolytic enzymes. Dousset, N.; Julia, A. M.; Chap, H.; Douste-Blazy, L. (Hop. Purpan, Toulouse, 31059, Fr.). Adv. Exp. Med. Biol., 243(Eicosanoids, Apolipoproteins, Lipoprotein Part. Atheroscler.), 255-61 (English) 1988. CODEN: AEMBAP. ISSN: 0065-2598.

AB The activity of **cholesteryl ester transfer protein** (**CETP**) in **rabbit** blood plasma was studied by monitoring the radiolabeled cholesteryl ester transfer from high-d. (HDL) to very-low-d. lipoproteins (VLDL). The data were related to HDL and VLDL fractional and chem. compn. and to lipoprotein and triacylglycerol lipases activities in **rabbits** rendered hyperlipemic by cyclophosphamide (I; 65 mg/kg i.v.). I sharply increased plasma levels of triglycerides, cholesterol, VLDL, and VLDL free cholesterol and cholesteryl esters. HDL cholesterol esters decreased, while free cholesterol was unchanged. Apoprotein and triglycerides were increased in both HDL and VLDL. Lipoprotein lipase-treated control VLDL increased the intake of cholesteryl esters, while those from treated **rabbits** decreased the intake. The transport protein structure was unchanged by I **treatment**, but the transfer activity with native lipoproteins was higher than in controls. I apparently changes lipoprotein fraction ratios and compn. and inhibits lipoprotein lipase, but does not influence liver triacylglycerol lipase. Combination of these changes increases the cholesteryl ester transfer between lipoprotein fractions in **rabbits** treated with I.

L12 ANSWER 24 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

87147784 EMBASE Document No.: 1987147784. Comparative molecular weight of **cholesteryl ester transfer protein** from cyclophosphamide- and irradiation-treated **rabbits**: Size determination by radiation inactivation method. Loudet A.-M.; Dousset N.; Potier M.; et al.. INSERM Unite 101, Biochimie des Lipides, Hopital Purpan, 31059 Toulouse, France. Medical Science Research 15/5 (251-252) 1987.

CODEN: MSCREJ. Pub. Country: United Kingdom. Language: English.

AB Previous results concerning the cholesteryl transfer protein (**CETP**) activity between HDL and VLDL have led us to determine the molecular weight (Mr) of this molecule. In fact, we have observed an increase of **CETP** activity in antimitotic (cyclophosphamide) treated **rabbit**. In order to evaluate the molecular size of this protein,

we have chosen the radiation inactivation method because this technique can determine in certain conditions the size of the functional unit in situ. Results showed that this molecule was not influenced by antimitotic **treatment** since we obtained a Mr of about 71,000 and 72,000 respectively for control and cyclophosphamide-treated **rabbits**. A similar value was obtained for **rabbits** after total whole-body irradiation. Since the molecular size by radiation inactivation corresponds to the subunit of the enzyme, we can conclude that the functional unit of this enzyme, i.e. the minimal assembly of structure required for biological activity, is the subunit.

L12 ANSWER 25 OF 25 MEDLINE DUPLICATE 6
86000670 Document Number: 86000670. PubMed ID: 4041478. Triacylglycerol increase in plasma very low density lipoproteins in cyclophosphamide-treated **rabbit**: relationship with cholesteryl ester transfer activity. Loudet A M; Dousset N; Perret B; Ierides M; Carton M; Douste-Blazy L. BIOCHIMICA ET BIOPHYSICA ACTA, (1985 Oct 2) 836 (3) 376-84. Journal code: A0W; 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB We have studied the cholesteryl ester transfer between HDL and VLDL in cyclophosphamide-treated **rabbits**, in order to explain the abnormal cholesteryl ester partition between these two lipoprotein classes. The hypertriglyceridemia caused by **treatment** with the drug was associated with cholesteryl ester- and triacylglycerol-rich VLDL and with HDL poor in esterified cholesterol but relatively enriched in triacylglycerol. These two lipoprotein classes were characterized by their chemical composition and by gel filtration chromatography. VLDL particles were slightly larger in size, compared with controls. Different transfer combinations were envisaged between these abnormal lipoproteins and control ones. The transfer study involved the plasma fraction of d greater than 1.21 g/ml containing the **cholesteryl ester transfer protein** (**CETP**). It appeared that the chemical composition of lipoproteins was responsible for the level of cholesteryl ester transfer between lipoproteins. Actually, when the cholesteryl ester acceptor lipoproteins (VLDL) were enriched in triacylglycerol, the transfer was enhanced. Therefore, the effect of lipolysis on the transfer has also been explored. Lipoprotein lipase seemed to enhance the transfer of cholesteryl ester from HDL to VLDL when these lipoproteins were normal, but an important decline was obtained when triacylglycerol-rich VLDL were lipolyzed. This study defines the relationship between lipoprotein chemical composition and transfer activity of cholesteryl ester from HDL to VLDL.

=> s l2 and simian

L13 32 L2 AND SIMIAN

=> dup remove l13

PROCESSING COMPLETED FOR L13
L14 9 DUP REMOVE L13 (23 DUPLICATES REMOVED)

=> d l14 1-9 cbib abs

L14 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS
1998:352957 Document No. 129:24159 A bicistronic adenovirus gene therapy vector for treating pathological conditions linked with dyslipoproteinemia. Benoit, Patrick; Duverger, Nicolas; Rouy, Didier; Seguret, Sandrine (Rhone-Poulenc Rorer S.A., Fr.; Benoit, Patrick;

Duverger, Nicolas; Rouy, Didier; Seguret, Sandrine). PCT Int. Appl. WO 9822606 A1 19980528, 50 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (French). CODEN: PIXXD2. APPLICATION: WO 1997-FR2043 19971113. PRIORITY: FR 1996-13969 19961115.

AB A replication-defective adenovirus carrying a bicistronic expression cassette for a pair of genes for proteins or enzymes involved in the transport and metab. of cholesterol that uses a strong promoter and an IRES sequence to achieve high-level expression of both genes is described.

Genes for apolipoprotein AI or AIV, cholesterol ester transfer protein, hepatic lipase, and lecithin cholesterol acetyltransferase are used in combinations. The invention further concerns plasmid constructs useful for prepg. these adenovirus, and cells transformed by these plasmids or adenovirus and pharmaceutical compns. contg. said adenovirus.

L14 ANSWER 2 OF 9 MEDLINE DUPLICATE 1

1998318463 Document Number: 98318463. PubMed ID: 9611161. Remodeling of the HDL in NIDDM: a fundamental role for **cholesteryl ester transfer protein**. Castle C K; Kuiper S L; Blake W L; Paigen B; Marotti K R; Melchior G W. (Pharmacia and Upjohn, Inc., Kalamazoo, Michigan 49001, USA.) AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Jun) 274 (6 Pt 1) E1091-8. Journal code: 3U8; 0370511. ISSN: 0002-9513. Pub. country: United States. Language: English.

AB When the Ay gene is expressed in KK mice, the yellow offspring (KKAy mice)

become obese, insulin resistant, hyperglycemic, and severely hypertriglyceridemic, yet they maintain extraordinarily high plasma high-density lipoprotein (HDL) levels. Mice lack the ability to redistribute neutral lipids among circulating lipoproteins, a process catalyzed in humans by **cholesteryl ester transfer protein** (**CETP**). To test the hypothesis that it is the absence of **CETP** that allows these hypertriglyceridemic mice to maintain high plasma HDL levels, **simian CETP** was expressed in the KKAy mouse. The KKAy-**CETP** mice retained the principal characteristics of KKAy mice except that their plasma HDL levels were reduced (from 159 +/- 25 to 25 +/- 6 mg/dl) and their free apolipoprotein A-I concentrations increased (from 7 +/- 3 to 22 +/- 6 mg/dl). These changes appeared to result from a **CETP**-induced enrichment of the HDL with triglyceride (from 6 +/- 2 to 60 +/- 18 mol of triglyceride/mol of HDL), an alteration that renders HDL susceptible to destruction by lipases. These data support the premise that **CETP**-mediated remodeling of the HDL is responsible for the low levels of that lipoprotein that accompany hypertriglyceridemic non-insulin-dependent diabetes mellitus.

L14 ANSWER 3 OF 9 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:432129 The Genuine Article (R) Number: ZQ830. Remodeling of the HDL in NIDDM: a fundamental role for **cholesteryl ester transfer protein**. Castle C K; Kuiper S L; Blake W L; Paigen B; Marotti K R; Melchior G W (Reprint). PHARMACIA & UPJOHN INC, 7252-209-4, KALAMAZOO, MI 49001 (Reprint); PHARMACIA & UPJOHN INC, KALAMAZOO, MI 49001; JACKSON LAB, BAR HARBOR, ME 04609. AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM (JUN 1998) Vol. 37, No. 6, pp. E1091-E1098. Publisher: AMER PHYSIOLOGICAL SOC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0193-1849. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB When the Ar gene is expressed in KK mice, the yellow offspring (KKA(y) mice) become obese, insulin resistant, hyperglycemic, and severely hypertriglyceridemic, yet they maintain extraordinarily high plasma

high-density lipoprotein (HDL) levels. Mice lack the ability to redistribute neutral lipids among circulating lipoproteins, a process catalyzed in humans by **cholesteryl ester transfer protein** (**CETP**). To test the hypothesis that it is the absence of **CETP** that allows these hypertriglyceridemic mice to maintain high plasma HDL levels, **simian CETP** was expressed in the KKA(y) mouse. The KKA(y)-**CETP** mice retained the principal characteristics of KKA(y) mice except that their plasma HDL levels were reduced (from 159 +/- 25 to 25 +/- 6 mg/dl) and their free apolipoprotein A-I concentrations increased (from 7 +/- 3 to 22 +/- 6 mg/dl). These changes appeared to result from a **CETP**-induced enrichment of the HDL with triglyceride (from 6 +/- 2 to 60 +/- 18 mol of triglyceride/mol of HDL), an alteration that renders HDL susceptible to destruction by lipases. These data support the premise that **CETP**-mediated remodeling of the HDL is responsible for the low levels of that lipoprotein that accompany hypertriglyceridemic non-insulin-dependent diabetes mellitus.

L14 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS

1998:460511 Document No. 129:239293 Reverse cholesterol transport and utilization of transgenic mice and transgenic rabbits to test protective genes against atherosclerosis development. Fruchart, Jean-Charles; Duriez, Patrick (Departement d'Atherosclerose, INSERM U325, Institute Pasteur, Lille, 59019, Fr.). Bull. Acad. Natl. Med. (Paris), 182(2), 233-249 (French) 1998. CODEN: BANMAC. ISSN: 0001-4079. Publisher: Academie Nationale de Medecine.

AB A review and discussion with 30 refs. Atherosclerosis is the leading cause of death in industrial societies. In France, 215 men out of 100,000 aged from 25 to 64 yr old suffered a myocardial infarction in 1992 and 67 men out of 100,000 died due to this disease. Hypercholesterolemia corresponding to a high LDL cholesterol level is an important risk factor of myocardial infarction. Nevertheless a low cholesterol level in the HDL fraction (frequently assocd. with an increase in triglycerides concns.) is a common abnormality found in patients with confirmed coronary artery disease. Therefore, in addn. to reducing triglycerides and LDL cholesterol levels, a therapeutic strategy consists of increasing the serum HDL cholesterol concn. in order to improve the reverse cholesterol transport. Apo A-I is the major protein of HDL. Studies in mice and rabbits transgenic for human apo A-I showed that over-expression of this protein in these animals resulted in an increase in the HDL cholesterol level. The serum of these animals contains a high concn. of particles contg. human apo A-I but not mouse apo A-II (LpA-I) and presents a higher ability to induce cellular cholesterol efflux than the serum of control mice. These alterations result in a redn. of atherosclerosis development when these animals are submitted to a cholesterol rich diet. Lecithin cholesterol acyl-transferase (LCAT) is a major enzyme in the metabolic cascade leading to the return of cholesterol to the liver. The metabolic role of LCAT is to esterify the free cholesterol of native HDL. Native HDL acquires free cholesterol during the transfer of cholesterol from the cell membrane to the particle during the cellular cholesterol efflux, which is the first step of the reverse cholesterol transport. Mice and rabbits transgenic for human LCAT have higher HDL-cholesterol levels. Transgenic rabbits, but not transgenic mice, are protected against diet induced atherosclerosis development. Nevertheless, cholesterol fed mice which are transgenic for both human LCAT and **simian** cholesteryl ester transfer (**CETP**) protein do not develop atherosclerosis. This data indicates that over-prodn. of LCAT reduces atherosclerosis when **CETP** is naturally (rabbit) or artificially (**CETP** transgenic mice) expressed in the animals. Gene therapy in mice induced by adenovirus-mediated transfer of human apo A-I and LCAT genes also

increased circulating apo A-I and LCAT. Therefore apo A-I and LCAT are two potential targets for gene therapy in patients with atherosclerosis assocd. with a low HDL cholesterol level.

L14 ANSWER 5 OF 9 MEDLINE DUPLICATE 2
1998040286 Document Number: 98040286. PubMed ID: 9374130. Relationship between lipoprotein lipase and high density lipoprotein cholesterol in mice: modulation by **cholesteryl ester transfer protein** and dietary status. Clee S M; Zhang H; Bissada N; Miao L; Ehrenborg E; Benlian P; Shen G X; Angel A; LeBoeuf R C; Hayden M R. (Department of Medical Genetics, University of British Columbia, Vancouver, Canada.) JOURNAL OF LIPID RESEARCH, (1997 Oct) 38 (10) 2079-89. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.
AB Plasma lipoprotein lipase (LPL) activity correlates with high density lipoprotein (HDL) cholesterol levels in humans. However, in several mouse models created either through transgenesis or targeted inactivation of LPL, no significant changes in HDL cholesterol values have been evident. One possible explanation for this species difference could be the absence of plasma **cholesteryl ester transfer protein** (**CETP**) activity in mice. To explore this possibility and further investigate interactions between LPL and **CETP** modulating HDL cholesterol levels in vivo, we examined the relationship between LPL activity and HDL levels in mice expressing the **simian CETP** transgene, compared with littermates not carrying the **CETP** gene. On a chow diet, increasing LPL activity was associated with a trend towards increased HDL levels (51 +/- 29 vs. 31 +/- 4 mg/dL highest vs. lowest tertiles of LPL activity, P = 0.07) in mice expressing **CETP**, while no such effects were seen in the absence of **CETP** (65 +/- 12 vs. 61 +/- 15 mg/ dL). Furthermore, in the presence of **CETP**, a significant positive correlation between LPL activity and HDL cholesterol was evident (r = 0.15, P = 0.006), while in the absence of **CETP** no such correlation was detected (r = 0.15, P = 0.36), highlighting the interactions between LPL and **CETP** in vivo. When mice were challenged with a high fat, high carbohydrate diet, strong correlations between LPL activity and HDL cholesterol were seen in both the presence (r = 0.45, P = 0.03) and absence (r = 0.73, P < 0.001) of **CETP**. Therefore, under altered metabolic contexts, such as those induced by dietary challenge, the relation between LPL activity and HDL cholesterol may also become evident. Here we have shown that both genetic and environmental factors may modulate the association between LPL activity and HDL cholesterol, and provide explanations for the absence of any changes in HDL values in mice either transgenic or with targeted disruption of the LPL gene.

L14 ANSWER 6 OF 9 MEDLINE DUPLICATE 3
96210602 Document Number: 96210602. PubMed ID: 8633025. Centripetal cholesterol flux from extrahepatic organs to the liver is independent of the concentration of high density lipoprotein-cholesterol in plasma. Osono Y; Woollett L A; Marotti K R; Melchior G W; Dietschy J M. (Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas 75235-8887, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Apr 30) 93 (9) 4114-9. Journal code: PV3; 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB High density lipoproteins (HDLs) play a role in two processes that include the amelioration of atheroma formation and the centripetal flow of cholesterol from the extrahepatic organs to the liver. This study tests

the hypothesis that the flow of sterol from the peripheral organs to the liver is dependent upon circulating HDL concentrations. Transgenic C57BL/6 mice were used that expressed variable amounts of **simian cholesteryl ester-transfer protein** (**CETP**). The rate of centripetal cholesterol flux was quantitated as the sum of the rates of cholesterol synthesis and low density lipoprotein-cholesterol uptake in the extrahepatic tissues. Steady-state concentrations of cholesterol carried in HDL (HDL-C) varied from 59 to 15 mg/dl and those of apolipoprotein AI from 138 to 65 mg/dl between the control mice (CETPc) and those maximally expressing the transfer protein (**CETP**+). There was no difference in the size of the extrahepatic cholesterol pools in the CETPc and **CETP**+ animals. Similarly, the rates of cholesterol synthesis (83 and 80 mg/day per kg, respectively) and cholesterol carried in low density lipoprotein uptake (4 and 3 mg/day per kg, respectively) were virtually identical in the two groups. Thus, under circumstances where the steady-state concentration of HDL-C varied 4-fold, the centripetal flux of cholesterol from the peripheral organs to the liver was essentially constant at approximately 87 mg/day per kg. These studies demonstrate that neither the concentration of HDL-C or apolipoprotein AI nor the level of **CETP** activity dictates the magnitude of centripetal cholesterol flux from the extrahepatic organs to the liver, at least in the mouse.

L14 ANSWER 7 OF 9 MEDLINE DUPLICATE 4

95096086 Document Number: 95096086. PubMed ID: 7798236. Co-expression of **cholesteryl ester transfer protein** and defective apolipoprotein E in transgenic mice alters plasma cholesterol distribution. Implications for the pathogenesis of type III hyperlipoproteinemia. Fazio S; Marotti K R; Lee Y L; Castle C K; Melchior G W; Rall S C Jr. (Gladstone Institute of Cardiovascular Disease, University of California, San Francisco 94141.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Dec 23) 269 (51) 32368-72. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Despite the definite etiologic link between apolipoprotein (apo) E mutations and type III hyperlipoproteinemia (HLP), it is not clear what additional factors are involved in the development of florid hyperlipidemia and how to explain the wide variability in the expression of the hyperlipidemic phenotype in carriers of receptor binding-defective apoE variants. The present study was designed to determine whether the overexpression of **cholesteryl ester transfer protein** (**CETP**), a plasma protein that transfers cholesteryl esters from the high density lipoproteins (HDL) to the very low density lipoproteins (VLDL) and whose activity is increased in hyperlipidemic states, plays a role in the development of hyperlipidemia and beta-VLDL accumulation in type III HLP. We produced double-transgenic mice that co-expressed high levels of **simian CETP** and either high or low levels of a human receptor binding-defective apoE variant, apoE(Cys-142). We previously reported that apoE(Cys-142) high-expresser mice showed spontaneous hyperlipidemia and accumulation of beta-VLDL, whereas the low-expresser mice showed only a modest increase in VLDL cholesterol. Co-expression of **CETP** induced a massive transfer of cholesteryl esters from the HDL to the VLDL in both lines of double-transgenic mice. As a result, HDL cholesterol and apoA-I levels were reduced to about 50% of normal, VLDL cholesterol increased 2.5-fold, and the cholesteryl ester content of VLDL reached values similar to those observed in human beta-VLDL. The ratio of defective to normal apoE in VLDL was unaffected by **CETP** co-expression and was higher in animals expressing high apoE levels. Finally, in spite of an increased

accumulation of beta-VLDL in the high-expresser mice, the VLDL of the low-expresser mice maintained pre-beta mobility upon co-expression of **CETP**. The results of this study demonstrate that the ratio of defective to normal apoE on the VLDL, rather than the cholesteryl ester content of VLDL, is the major factor determining the development of severe hyperlipidemia and the formation and accumulation of beta-VLDL in type III HLP.

L14 ANSWER 8 OF 9 MEDLINE DUPLICATE 5
94179173 Document Number: 94179173. PubMed ID: 8132527. Apolipoprotein A-I metabolism in **cholesteryl ester transfer protein** transgenic mice. Insights into the mechanisms responsible for low plasma high density lipoprotein levels. Melchior G W; Castle C K; Murray R W; Blake W L; Dinh D M; Marotti K R. (Department of Metabolic Diseases Research, Upjohn Laboratories, Kalamazoo, Michigan 49001.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Mar 18) 269 (11) 8044-51. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Expression of **simian cholesteryl ester transfer protein** (**CETP**) in C57BL/6 mice causes the animals' high density lipoprotein (HDL) levels to decrease. The purpose of these studies was to determine how **CETP** expression caused that reduction. Chemical analysis showed that the HDL of the **CETP** transgenic mice had about twice as much triglyceride and only about 60% as much cholesteryl ester as the HDL from the C57BL/6 mice. Both strains of mouse had high levels of a circulating lipase. When plasma from the mice was incubated at 37 degrees C for 5 h, the triglycerides in the HDL were hydrolyzed, and apoA-I was shed from the particle. However, apoA-I was shed from the **CETP** HDL more rapidly than it was shed from the C57BL/6 HDL. Because "free" apoA-I is rapidly cleared by the kidney, increased production of free apoA-I would be expected to shorten the average life span of apoA-I in the mouse. Kinetic analyses indicated that the life span of apoA-I was significantly reduced in the **CETP** transgenic mice. It was concluded that **CETP** expression enriched the core of the HDL with triglyceride, which rendered it vulnerable to lipolysis, causing apoA-I to be shed from the particle. That shortened the life span of apoA-I in the **CETP** mice, which led to lower plasma levels of the protein.

L14 ANSWER 9 OF 9 MEDLINE DUPLICATE 6
93302855 Document Number: 93302855. PubMed ID: 8316302. Severe atherosclerosis in transgenic mice expressing **simian cholesteryl ester transfer protein**. Marotti K R; Castle C K; Boyle T P; Lin A H; Murray R W; Melchior G W. (Molecular Biology Research and Metabolic Diseases Research, Upjohn Laboratories, Kalamazoo, Michigan 49001.) NATURE, (1993 Jul 1) 364 (6432) 73-5. Journal code: NSC; 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) is a plasma protein that mediates the exchange of neutral lipids among the lipoprotein. Because the principal core lipid of very-low-density lipoprotein (VLDL) is triglyceride and that of high-density lipoprotein (HDL) is cholesterol ester, **CETP** mediates a 'heteroexchange' of cholesterol ester for triglyceride between those lipoproteins. As a result, animals that express **CETP** tend to have higher VLDL and low-density lipoprotein (LDL) cholesterol levels, whereas those with no **CETP** activity tend to have high HDL

cholesterol levels. Because VLDL and LDL are associated with the progression of atherosclerosis, and HDL are considered anti-atherogenic, **CETP** could be an 'atherogenic' protein, that is, given the other conditions required for atherosclerosis to develop, expression of **CETP** would accelerate the rate at which the arterial lesions progress. We report here that transgenic mice expressing **CETP** had much worse atherosclerosis than did non-expressing controls, and we suggest that the increase in lesion severity was due largely to **CETP**-induced alterations in the lipoprotein profile.

=> s l2 and mouse

L15 461 L2 AND MOUSE

=> s l15 and treatment

L16 33 L15 AND TREATMENT

=> dup remove l16

PROCESSING COMPLETED FOR L16
L17 22 DUP REMOVE L16 (11 DUPLICATES REMOVED)

=> d l17 1-22 cbib abs

L17 ANSWER 1 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:563015 The Genuine Article (R) Number: 451VP. **Cholesteryl ester transfer protein** biosynthesis and cellular cholesterol homeostasis are tightly interconnected. Izem L; Morton R E (Reprint). Cleveland Clin Fdn, Dept Cell Biol, Lerner Res Inst, 9500 Euclid Ave, NC10, Cleveland, OH 44195 USA (Reprint); Cleveland Clin Fdn, Dept Cell Biol, Lerner Res Inst, Cleveland, OH 44195 USA. JOURNAL OF BIOLOGICAL CHEMISTRY (13 JUL 2001) Vol. 276, No. 28, pp. 26534-26541. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0021-9258. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Cholesteryl ester transfer protein** (**CETP**) mediates triglyceride and cholesteryl eater (CE) transfer between lipoproteins, and its activity is strongly modulated by dietary cholesterol. To better understand the regulation of **CETP** synthesis and the relationship between **CETP** levels and cellular lipid metabolism, we selected the SW872 adipocytic cell line as a model. These cells secrete **CETP** in a time-dependent manner at levels exceeding those observed for Caco-2 or HepG2 cells. The addition of LDL, 25OH-cholesterol, oleic acid, or acetylated LDL to SW872 cells increased **CETP** secretion (activity and mass) up to 6-fold. In contrast, **CETP** production was decreased by almost 60% after **treatment** with lipoprotein-deficient serum or P-cyclodextrin, These effects, which were paralleled by changes in **CETP** mRNA, show that **CETP** biosynthesis in SW872 cells directly correlates with cellular lipid status. To investigate a possible, reciprocal relationship between **CETP** expression and cellular lipid homeostasis, **CETP** biosynthesis in SW872 cells was suppressed with **CETP** antisense oligonucleotides. Antisense oligonucleotides reduced **CETP** secretion (activity and mass) by 60% compared with sense-treated cells. When **CETP** synthesis was suppressed for 24 h, triglyceride synthesis was unchanged, but cholesterol biosynthesis was reduced by 20%, and acetate incorporation into CE increased 31%, After 3 days of suppressed **CETP** synthesis, acetate incorporation into

the CE pool increased 3-fold over control. This mirrored a similar increase in CE mass. The efflux of free cholesterol to HDL was the same in sense and antisense-treated cells; however, HDL-induced CE hydrolysis in antisense-treated cells was diminished a-fold even though neutral CE hydrolase activity was unchanged. Thus, **CETP**-compromised SW872 cells display a phenotype characterized by inefficient mobilization of CE stores leading to CE accumulation. These results strongly suggest that **CETP** expression levels contribute to normal cholesterol homeostasis in adipocytic cells. Overall, these studies demonstrate that lipid homeostasis and **CETP** expression are tightly coupled.

L17 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2002 ACS
2001:367830 Document No. 135:120741 Analysis of glomerulosclerosis and atherosclerosis in lecithin cholesterol acyltransferase-deficient **mice**. Lambert, Gilles; Sakai, Naohiko; Vaisman, Boris L.; Neufeld, Edward B.; Marteyn, Benoit; Chan, Chi-Chao; Paigen, Beverly; Lupia, Enrico; Thomas, Alton; Striker, Liliane J.; Blanchette-Mackie, Joan; Csako, Gyorgy; Brady, John N.; Costello, Rene; Striker, Gary E.; Remaley, Alan T.; Brewer, H. Bryan, Jr.; Santamarina-Fojo, Silvia (Molecular Disease Branch, NHLBI, National Institutes of Health, Bethesda, MD, 20892, USA). J. Biol. Chem., 276(18), 15090-15098 (English) 2001. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.
AB To evaluate the biochem. and mol. mechanisms leading to glomerulosclerosis and the variable development of atherosclerosis in patients with familial lecithin cholesterol acyl transferase (LCAT) deficiency, we generated LCAT knockout (KO) **mice** and cross-bred them with apolipoprotein (apo) E KO, low d. lipoprotein receptor (LDLr) KO, and **cholesteryl ester transfer protein** (**CETP**) transgenic **mice**. LCAT-KO **mice** had normochromic normocytic anemia with increased reticulocyte and target cell counts as well as decreased red blood cell osmotic fragility. A subset of LCAT-KO **mice** accumulated lipoprotein X and developed protein-uria and glomerulosclerosis characterized by mesangial cell proliferation, sclerosis, lipid accumulation, and deposition of electron dense material throughout the glomeruli. LCAT deficiency reduced the plasma high d. lipoprotein (HDL) cholesterol (-70 to -94%) and non-HDL cholesterol (-48 to -85%) levels in control, apoE-KO, LDLr-KO, and **cholesteryl ester transfer protein**-Tg **mice**. Transcriptome and Western blot anal. demonstrated up-regulation of hepatic LDLr and apoE expression in LCAT-KO **mice**. Despite decreased HDL, aortic atherosclerosis was significantly reduced (-35% to -99%) in all **mouse** models with LCAT deficiency. Our studies indicate (i) that the plasma levels of apoB contg. lipoproteins rather than HDL may det. the atherogenic risk of patients with hypoalphalipoproteinemia due to LCAT deficiency and (ii) a potential etiol. role for lipoproteins X in the development of glomerulosclerosis in LCAT deficiency. The availability of LCAT-KO **mice** characterized by lipid, hematol., and renal abnormalities similar to familial LCAT deficiency patients will permit future evaluation of LCAT gene transfer as a possible **treatment** for glomerulosclerosis in LCAT-deficient states.

L17 ANSWER 3 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001404056 EMBASE Novel agents for managing dyslipidaemia. Best J.D.; Jenkins A.J.. J.D. Best, University of Melbourne, Department of Medicine, St

Vincent's Hospital Melbourne, Melbourne, Vic. 3065, Australia. jdbest@unimelb.edu.au. Expert Opinion on Investigational Drugs 10/11 (1901-1911) 2001.
Refs: 100.
ISSN: 1354-3784. CODEN: EOIDER. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB An elevated low-density lipoprotein (LDL) cholesterol level is a strong predictor of coronary heart disease (CHD) risk. Over the past seven years, equally strong evidence has accumulated that lowering LDL cholesterol with HMG-CoA reductase inhibitors or statins reduces CHD risk and there is now widespread use of these agents for the primary and secondary prevention of CHD. **Treatment** issues remain regarding the appropriate degree of LDL cholesterol reduction and whether, in people with very high levels, it would be preferable to achieve the LDL cholesterol goal with a powerful statin alone or combined with an agent that lowers LDL cholesterol by a different mechanism. The main focus in the development of novel agents is the patient with low high-density lipoprotein (HDL) cholesterol, usually associated with hypertriglyceridaemia. Already prevalent as a risk factor for CHD, this abnormality has been linked with insulin resistance, which is likely to increase greatly over the next decade, along with increasing obesity and diabetes. Agents that have potent HDL cholesterol raising capacity include **cholesteryl ester transfer protein** (**CETP**) inhibitors, retinoid X receptor (RXR) selective agonists, specific peroxisome proliferator-activated receptor (PPAR) agonists and oestrogen-like compounds. Another area of development involves agents that will lower both cholesterol and triglyceride levels, such as partial inhibitors of microsomal triglyceride transfer protein (MTP) and perhaps squalene synthase inhibitors and agonists of AMP kinase. Future emphasis will be on correcting all lipid abnormalities for the prevention of CHD, not just lowering LDL cholesterol.

L17 ANSWER 4 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:391390 The Genuine Article (R) Number: 428QP. **Cholesteryl ester transfer protein** inhibitors. Shinkai H (Reprint). JT Inc, Cent Pharmaceut Res Inst, 1-1 Murasaki Cho, Takatsuki, Osaka 5691125, Japan (Reprint); JT Inc, Cent Pharmaceut Res Inst, Takatsuki, Osaka 5691125, Japan. EXPERT OPINION ON THERAPEUTIC PATENTS (MAY 2001) Vol. 11, No. 5, pp. 739-745. Publisher: ASHLEY PUBLICATIONS LTD. UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND. ISSN: 1354-3776. Pub. country: Japan. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB As well as hypercholesterolaemia, low levels of high-density lipoprotein cholesterol (HDL;C) are critical risk factors for atherosclerosis and coronary heart disease (CHD). Although fibrate, simvastatin and niacin can be used for the **treatment** of a low HDL-C level, their effects, however, are not wholly satisfactory. Thus, better drugs for the elevation of HDL-C are desired. Among the many methods that mag; be used to raise HDL-C levels, this review focuses on small molecule inhibitors of **cholesteryl ester transfer protein** (**CETP**) and summarises recent patent and journal data.

L17 ANSWER 5 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:609792 The Genuine Article (R) Number: 454YZ. Plasma **cholesteryl ester transfer protein** and lipoprotein levels during **treatment** of growth hormone-deficient adult humans. Carrilho A J F; Cunha-Neto M B; Nunes V S; Lottenberg A M P; Medina W L; Nakandakare E R; Musolino N R; Bronstein M D; Quintao E C R (Reprint).

Univ Sao Paulo, Sch Med, Lipids Lab LIM 10, Av Dr Arnaldo 455, Room 3317, BR-01246903 Sao Paulo, Brazil (Reprint); Univ Sao Paulo, Sch Med, Lipids Lab LIM 10, BR-01246903 Sao Paulo, Brazil; Univ Sao Paulo, Sch Med, Dept Psychiat, Neurosurg Div, Neuroendocrine Unit, BR-01246903 Sao Paulo, Brazil. LIPIDS (JUN 2001) Vol. 36, No. 6, pp. 549-554. Publisher: AMER OIL CHEMISTS SOC A O C S PRESS. 1608 BROADMOOR DRIVE, CHAMPAIGN, IL 61821-0489 USA. ISSN: 0024-4201. Pub. country: Brazil. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The incidence of atherosclerosis is increased in growth hormone (GH) deficient-individuals. Nonetheless, the antiatherogenic benefits of GH replacement therapy remain uncertain. In this study the effect of human recombinant growth hormone (hrGH) replacement therapy administered to GH-deficient adults on the plasma **cholesteryl ester transfer protein** (**CETP**) concentration and activity was analyzed. These findings were related to changes in the concentrations of the plasma lipoproteins. The hrGH was administered for 12 mon to human GH-deficient patients (n = 13; 8 men, 5 women). During the study plasma lipoproteins were separated by ultracentrifugation, and plasma cholesterol esterification rate (CER), endogenous **CETP** activity, and **CETP** concentration were measured. GH replacement therapy transiently (at 3 mon) lowered plasma concentration of **CETP** and low density lipoprotein-cholesterol (LDL-C) and raised total triglycerides. Furthermore, hrGH permanently increased both the plasma lipoprotein(a) [Lp(a)] concentration, which is known as atherogenic, and the proportion of cholesteryl ester in the high density lipoprotein(2) (HDL2) particles, which is potentially atheroprotective. The simultaneous decrease of the plasma **CETP** and LDL-C concentrations elicited by hrGH indicated a close relationship between LDL metabolism and the regulation of the **CETP** gene expression. Endogenous **CETP** activity and the CER were not modified because these parameters are regulated in opposite ways by plasma levels of triglycerides; that is, CER increased and **CETP** decreased.

L17 ANSWER 6 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

2000:929883 The Genuine Article (R) Number: 379AL. Human apolipoprotein C-I accounts for the ability of plasma nigh density lipoproteins to inhibit the **cholesteryl ester transfer protein** activity. Gautier T; Masson D; deBarros J P P; Athias A; Gambert P; Aunis D; MetzBoutigue M H; Lagrost L (Reprint). HOP BOCAGE, INSERM U498, LAB BIOCHIM LIPOPROT, BP1542, F-21034 DIJON, FRANCE (Reprint); HOP BOCAGE, INSERM U498, LAB BIOCHIM LIPOPROT, F-21034 DIJON, FRANCE; CNRS, CTR NEUROCHIM, INSERM U338, LAB BIOL COMMUN CELLULAIRE, F-67084 STRASBOURG, FRANCE. JOURNAL OF BIOLOGICAL CHEMISTRY (1 DEC 2000) Vol. 275, No. 48, pp. 37504-37509. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0021-9258. Pub. country: FRANCE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The aim of the present study was to identify the protein that accounts for the **cholesteryl ester transfer protein** (**CETP**)-inhibitory activity that is specifically associated with human plasma high density lipoproteins (HDL). To this end, human HDL apolipoproteins were fractionated by preparative polyacrylamide gradient gel electrophoresis, and 30 distinct protein fractions with molecular masses ranging from 80 down to 2 kDa were tested for their ability to inhibit **CETP** activity. One single apolipoprotein fraction was able to completely inhibit **CETP** activity. The N-terminal sequence of the 6-kDa protein inhibitor matched the N-terminal sequence of human apoC-I, the inhibition was completely blocked by specific anti-apolipoprotein C-I antibodies, and mass spectrometry

analysis confirmed the identity of the isolated inhibitor with full-length
human apoC-I. Pure apoC-I was able to abolish **CETP** activity in a concentration-dependent manner and with a high efficiency (IC50 = 100 nmol/liter). The inhibitory potency of total delipidated HDL apolipoproteins completely disappeared after a **treatment** with anti-apolipoprotein C-I antibodies, and the apoC-I deprivation of native plasma HDL by immunoaffinity chromatography produced a mean 43% rise in cholesteryl ester transfer rates. The main localization of apoC-I in HDL and not in low density lipoprotein in normolipidemic plasma provides further support for the specific property of HDL in inhibiting **CETP** activity.

L17 ANSWER 7 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
2000340498 EMBASE Differential expression of **cholesteryl ester transfer protein** in the liver and plasma of fasted and fed transgenic **mice**. MacLean P.S.; Vadlamudi S.; Hao E.; Barakat H.A.. Dr. H. Barakat, Department of Biochemistry, East Carolina Univ. School of Med., Greenville, NC 27858, United States. Journal of Nutritional Biochemistry 11/6 (318-325) 2000.
Refs: 31.
ISSN: 0955-2863. CODEN: JNBIEL.
Publisher Ident.: S 0955-2863(00)00084-X. Pub. Country: United States.
Language: English. Summary Language: English.
AB Because **cholesteryl ester transfer protein** (**CETP**) is considered a potential target in the **treatment** of atherosclerosis, several reports have focused on the regulation of this enzyme, and there is evidence that insulin may be a regulatory factor. The present study examines the differential expression of the human **CETP** gene between physiologic conditions that are accompanied by low (fasted) and high (fed) insulin levels. **CETP** expression was examined in plasma and tissues of transgenic **mice** expressing the human **CETP** minigene after 12 hours of fasting (n = 20) or ad libitum feeding (n = 20) with normal **mouse** chow. Plasma cholesteryl ester transfer activity (CETA) was 20% higher in fed than in fasted **mice**, reflecting higher levels of **CETP** ($P < 0.05$). This observation was accompanied by higher liver mRNA in fed **mice** (100%, $P < 0.05$), as determined by ribonuclease protection assays, as well as by higher CETA (23%, $P < 0.05$) and **CETP** mass (29%, $P < 0.05$) in the particulate fraction of liver homogenates. These parameters of liver **CETP** expression correlated well with each other, as well as with plasma CETA. **CETP** in the liver particulate fraction was found as a doublet (approximately 70 and 65 kDa), which resolved to a single band (approximately 60 kDa) upon deglycosylation. No differences in **CETP** expression were observed in pooled adipose tissue samples from fed and fasted **mice**. Insulin and glucose were not related to any plasma or tissue parameter of **CETP** expression. In summary, the concerted, differential expression of **CETP** in the liver of fed and fasted transgenic **mice** appears to contribute to higher plasma **CETP** levels in fed **mice**, but the precise role of insulin and glucose in regulating **CETP** expression under fasted and fed conditions needs to be defined. (C) Elsevier Science Inc. 2000.

L17 ANSWER 8 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000326614 EMBASE Antiatherogenic effect of the extract of Allium victorialis on the experimental atherosclerosis in the rabbit and transgenic **mouse**. Tae Gyn Kim; Seung Hee Kim; Soeg Youn Kang; Ki Kyung Jung; Don Ha Choi; Yong Bok Park; Jong Hoon Ryu; Hyung Mee Han. H.M. Han, Natl. Inst. of Toxicological Res., Korea Food and Drug Administration, Seoul 122-704, Korea, Republic of. Korean Journal of Pharmacognosy 31/2 (149-156) 2000.

Refs: 25.
ISSN: 0253-3073. CODEN: SYHJAM. Pub. Country: Korea, Republic of.
Language: Korean. Summary Language: English.

AB Atherosclerosis is emerging as one of the major causes of death in Korea as well as Western societies. In the present study, hypocholesterolemic and antiatherogenic effects of the ethanol extract of Allium victorialis Makino was investigated using the conventional rabbit and the **cholesteryl ester transfer protein** (**CETP**)-transgenic **mouse** model. Hypercholesterolemia was induced by feeding high cholesterol diet to the animals for 30 days and they were then fed with high cholesterol diet containing 0.5% of the A. victorialis extract for additional 30 (or 40) days. In the experiment using rabbits, **treatment** with the A. victorialis extract significantly decreased plasma total cholesterol, low density lipoprotein (LDL)-cholesterol, triglyceride levels and lipid peroxidation compared to those in the control group. Total cholesterol contents in the liver and the heart were also significantly decreased. Lipid staining of the aorta isolated from the rabbits showed that **treatment** with the A. victorialis extract decreased formation of atheromatous plaques on the intima of the aorta. In the experiment employing **CETP** transgenic **mouse** model, **treatment** with the A. victorialis extract decreased the levels of plasma total cholesterol and the tissue triglyceride levels in the heart. These results demonstrated that the ethanol extract of A. victorialis lowered serum cholesterol levels, tissue lipid contents and accumulation of cholesterol in the artery.

L17 ANSWER 9 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

2000:686723 The Genuine Article (R) Number: 351CE. Insulin does not regulate the promoter of **Cholesteryl Ester Transfer Protein** (**CETP**) in HIRc/pCETP-CAT cells. MacLean P S; Barakat H A (Reprint). E CAROLINA UNIV, SCH MED, DEPT BIOCHEM, GREENVILLE, NC 27858 (Reprint); E CAROLINA UNIV, SCH MED, DEPT BIOCHEM, GREENVILLE, NC 27858. MOLECULAR AND CELLULAR BIOCHEMISTRY (AUG 2000) Vol. 211, No. 1-2, pp. 1-7. Publisher: KLUWER ACADEMIC PUBL. SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS. ISSN: 0300-8177. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Cholesteryl ester transfer protein** (**CETP**) is a plasma enzyme involved in cholesterol metabolism. As a potential target in the **treatment** of atherosclerosis, a number of studies have focused how this enzyme is regulated. It has been postulated that insulin may regulate **CETP** gene expression, and these effects may be mediated through CCAAT/enhancer binding protein alpha (C/EBP alpha). The present study examines the effects of insulin on the activity of the **CETP** promoter in rat fibroblasts expressing the human insulin receptor (HIRc). HIRc cells were stably transfected with a chimeric construct containing 3.2 kb of the **CETP** promoter attached to the bacterial chloramphenicol acyltransferase gene (pCETP-CAT) without significantly affecting the expression of the insulin receptor. CAT activity was 8-fold higher in cultured HIRc/pCETP-CAT in the presence of 100 mg/dL LDL cholesterol, than those cultured without cholesterol ($p < 0.05$). However, culturing these cells in the presence of 100 nM insulin did not result in any change in CAT activity when compared to control cells. In HIRc/pCETP-CAT cells transiently transfected with a construct that constitutively expressed C/EBP alpha protein, a 3-fold increase in CAT activity was observed when compared to cells transiently transfected with non-specific DNA ($p < 0.05$). However, no observable effect on the **CETP** promoter was observed in the presence of insulin. Thus, in HIRc/pCETP-CAT cells, we were unable to substantiate the hypothesis that insulin regulates

CETP gene transcription. These results suggest that the effects of insulin on **CETP** expression regulation may be downstream of transcription.

L17 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2002 ACS
1999:282118 Document No. 130:310673 Xenogeneic **cholesteryl ester transfer protein** (**CETP**) for modulation of **CETP** activity in **treatment** of atherosclerosis. Rittershaus, Charles W.; Thomas, Lawrence J. (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.
AB Methods for modulating **cholesteryl ester transfer protein** (**CETP**) activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based vaccine for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

L17 ANSWER 11 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:680360 The Genuine Article (R) Number: 231RM. Opposite effects on serum **cholesteryl ester transfer protein** levels between long-term **treatments** with pravastatin and probucol in patients with primary hypercholesterolemia and xanthoma. Inazu A (Reprint); Koizumi J; Kajinami K; Kiyohar T; Chichibu K; Mabuchi H. KANAZAWA UNIV, SCH MED, DEPT INTERNAL MED 2, TAKARA MACHI 13-1, KANAZAWA, ISHIKAWA 920864, JAPAN (Reprint); KANAZAWA UNIV, SCH HLTH SCI, DEPT CLIN LAB SCI, KANAZAWA, ISHIKAWA 920094, JAPAN; KANAZAWA UNIV HOSP, DEPT GEN MED, KANAZAWA, ISHIKAWA 920864, JAPAN; CHUGAI PHARMACEUT CO LTD, DIAGNOST RES LABS, DIAGNOST LAB, TOKYO, JAPAN. ATHEROSCLEROSIS (AUG 1999) Vol. 145, No. 2, pp. 405-413. Publisher: ELSEVIER SCI IRELAND LTD. CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND. ISSN: 0021-9150. Pub. country: JAPAN. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Long-term effects of pravastatin and probucol on serum **cholesteryl ester transfer protein** (**CETP**) and xanthoma/xanthelasma size were compared. Twenty-three patients with primary hypercholesterolemia and xanthoma/xanthelasma, including 11 patients with heterozygous familial hypercholesterolemia, were treated with pravastatin (20 mg/day) or probucol (1000 mg/day) for 24 months. Serum **CETP** levels were measured by sandwich ELISA. In 11 patients (six men and five women, 55 +/- 2 [SE] yr) treated with pravastatin, serum cholesterol levels decreased from 262 +/- 13 to 229 +/- 13 mg/dl during the 24-month **treatment** period (P = 0.05). Serum HDL cholesterol levels were not changed. Serum **CETP** levels decreased from 2.5 +/- 0.2 to 2.0 +/- 0.2 mu g/ml (- 21%, P = 0.002). By contrast, in 12 patients (four men and eight women, 57 +/- 4 year) treated with probucol, serum cholesterol levels did not significantly decrease from 236 +/- 11 to 207 +/- 13 mg/dl. Serum HDL cholesterol levels decreased from 44 +/- 2 to 30 +/- 2 mg/dl (P = 0.009). Serum **CETP**

levels increased from 2.3 +/- 0.1 to 2.8 +/- 0.2 mu g/ml (+ 23%, P = 0.02), Xanthelasma regression was found in two of four patients (50%) each
treated with pravastatin and probucol, respectively. In contrast, Achilles' tendon xanthoma regressed in four of five patients (80%) treated
with pravastatin, but only in two of five patients (40%) treated with probucol. Patients with xanthoma/xanthelasma regression after 2 years **treatment** had higher baseline levels of serum **CETP** than
those without regression (2.7 +/- 0.2 mu g/ml [n = 9] versus 2.1 +/- 0.2 mu g/ml [n = 7], P = 0.05), Serial changes in serum **CETP** levels during **treatment** with pravastatin and probucol were discordant, but not related to the degree of xanthoma regression. However, higher level of serum HDL3 cholesterol was an independent factor in the smaller size of Achilles' tendon xanthoma at baseline. In addition, higher levels of serum HDL3 triglyceride on lipid-lowering therapy (6 months) appear to be a common predictor of regression of Achilles' tendon xanthoma in the **treatment** with either pravastatin or probucol.

L17 ANSWER 12 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:60305 The Genuine Article (R) Number: 154VW. The hepatic uptake of rat high-density lipoprotein cholesteryl ester is delayed after **treatment** with **cholesteryl ester transfer protein**. Botham K M; Avella M; Cantafora A; Bravo E (Reprint). IST SUPER SANITA, LAB METAB & BIOCHIM PATOL, VIALE REGINA ELENA 299, I-00161 ROME, ITALY (Reprint); IST SUPER SANITA, LAB METAB & BIOCHIM PATOL, I-00161 ROME, ITALY; UNIV LONDON ROYAL VET COLL, DEPT VET BASIC SCI, LONDON NW1 0TU, ENGLAND. PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE (JAN 1999) Vol. 220, No. 1, pp. 31-38. Publisher: BLACKWELL SCIENCE INC. 350 MAIN ST, MALDEN, MA 02148. ISSN: 0037-9727. Pub. country: ITALY; ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The effects of **cholesteryl ester transfer protein** (**CETP**) on the direct uptake of HDL cholesteryl ester by the liver was investigated using the rat in vivo and the isolated perfused rat liver as experimental models, Rat plasma was incubated with [H-3]cholesterol in the presence or absence of partially purified human **CETP** far 18 hr and [H-3]cholesteryl ester-labeled HDL was then isolated by ultracentrifugation, The **CETP**-treated as compared to untreated HDL showed a small shift toward a lower density in the peak of lipoprotein cholesterol, suggesting that the HDL particle size was increased, After injection of the labeled HDL into rats in vivo, more radioactivity remained in the plasma after 60 min when the **CETP** -treated preparation was used, but the amounts found in the liver and secreted in the bile were not significantly different from those obtained with the untreated HDL, The distribution of the label remaining in the plasma after 60 min between different density fractions corresponding to HDL subclasses suggested that the uptake of HDL, and HDL, was delayed by **CETP treatment**. Radioactivity from **CETP** -treated HDL was also removed from the perfusate of isolated perfused rat livers more slowly than that from untreated HDL, and in this case the amount found in the liver after 60 min was significantly lower, These findings indicate that **treatment** with **CETP** has a direct inhibitory effect on the clearance of rat HDL cholesteryl ester from the blood and its uptake by the liver.

L17 ANSWER 13 OF 22 MEDLINE DUPLICATE 2
1998421851 Document Number: 98421851. PubMed ID: 9751231. Role of female sex steroids in regulating **cholesteryl ester transfer protein** in transgenic **mice**. Vadlamudi S; MacLean P; Green T; Shukla N; Bradfield J; Vore S; Barakat H. (Department of Biochemistry, School of Medicine East Carolina University,

Greenville, NC 27858, USA.) METABOLISM: CLINICAL AND EXPERIMENTAL, (1998 Sep) 47 (9) 1048-51. Journal code: MUM; 0375267. ISSN: 0026-0495. Pub. country: United States. Language: English.

AB The role of sex steroids in the regulation of **cholesteryl ester transfer protein** (**CETP**) was examined in the following groups of female transgenic **mice** carrying the human **CETP** gene: (1) normal, (2) ovariectomized, (3) ovariectomized and treated with estrogen; (4) ovariectomized and treated with progesterone; (5) ovariectomized and treated with both hormones, and (6) ovariectomized and treated with tamoxifen. **CETP** activity was measured in the plasma, and in the particulate and the soluble fractions of liver, muscle, and adipose tissue. Human **CETP** specific activity was determined by taking the difference of cholesterol ester transfer in the presence and absence of an antibody (TP2) against human **CETP** Ovariectomy reduced hormone levels, but did not completely abolish them from the circulation. Plasma **CETP** activity was significantly reduced in the tamoxifen group. There were significant reductions in **CETP** in liver homogenate and the soluble fraction, as well as in the particulate fraction of adipose with ovariectomy. Hormone replacement did not restore **CETP** activity in either the plasma or the tissues. Tamoxifin **treatment** resulted in a decrease in **CETP** activity in both fractions of liver, but had no effect on adipose. In the soluble fraction of adipose tissue and both fractions of muscle, only trace **CETP** activity was detected. We conclude that (1) minimal amounts of sex steroid hormones may be sufficient to affect **CETP** expression; (2) the effects of sex steroid hormones vary among tissues; and (3) in addition to the sex steroids, factor(s) from the ovary are needed for the full expression of **CETP** in this animal model.

L17 ANSWER 14 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:612414 The Genuine Article (R) Number: 107RF. Effects of vitamin E and HMG-CoA reductase inhibition on **cholesteryl ester transfer protein** and lecithin-cholesterol acyltransferase in hypercholesterolemia. Napoli C (Reprint); Leccese M; Palumbo G; deNigris F; Chiariello P; Zuliani P; Somma P; DiLoreto M; DeMatteis C; Cacciatore F; Abete P; Liguori A; Chiariello M; DArmiento F P. VIA B FALCOMATA 5, I-80128 NAPLES, ITALY (Reprint); UNIV NAPLES FEDERICO II, DEPT CLIN & EXPT MED, NAPLES, ITALY; UNIV NAPLES FEDERICO II, INST INTERNAL MED CARDIOL GERIATR CLIN IMMUNOL, DIV GERIATR, NAPLES, ITALY; UNIV NAPLES FEDERICO II, INST PATHOL, NAPLES, ITALY; UNIV NAPLES FEDERICO II, DEPT CELLULAR & MOL BIOL & PATHOL L CALIFANO, NAPLES, ITALY; PELLEGRINI HOSP, DIV CARDIOL CCU, NAPLES, ITALY; POLICLIN CASILINO, DEPT MED, ROME, ITALY; HOSP ARIENZO S FELICE, DIV CARDIOL, CASERTA, ITALY; UNIV NAPLES FEDERICO II, INST INTERNAL MED CARDIOL GERIATR CLIN IMMUNOL, DIV CARDIOL, NAPLES, ITALY. CORONARY ARTERY DISEASE (16 JUL 1998) Vol. 9, No. 5, pp. 257-264. Publisher: RAPID SCIENCE PUBLISHERS. 2-6 BOUNDARY ROW, LONDON SE1 8NH, ENGLAND. ISSN: 0954-6928. Pub. country: ITALY. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background The enzyme lecithin-cholesterol acyl transferase (LCAT) esterifies free cholesterol on high-density lipoprotein (HDL) and the **cholesteryl ester transfer protein** (**CETP**) transfers cholesteryl esters to very-low-density lipoproteins (VLDL) and low-density lipoproteins (LDL). Using statins, contradictory findings have been made regarding **CETP** activity in normolipidemic individuals and in those with familial dysbetalipoproteinemia. In contrast, LCAT activity appears to be unaffected by simvastatin. Antioxidants have also been proposed for use in

anti-atherosclerotic **treatment**, because the oxidation of LDL may have a key role in the pathophysiology of atherogenesis.

Objective To investigate, in hypercholesterolemic patients, whether a combination of pravastatin with the antioxidant, vitamin E, has greater effects on the activity of **CETP** and of LCAT than does pravastatin alone.

Methods This placebo-diet-controlled multicenter trial included 220 hypercholesterolemic patients who were assigned randomly to groups to receive: diet and 20-40 mg pravastatin (n = 52), diet and pravastatin in combination with 100 mg/day vitamin E (100 IU) as DL-alpha-tocopherol (n = 56), diet and alpha-tocopherol (n = 60), or diet associated with placebo (n = 52). Plasma LCAT activity was determined using excess exogenous substrate, containing [H-3]cholesterol. Plasma **CETP** activity was measured in the supernatant fraction after precipitation of endogenous apo B-containing lipoproteins with phosphotungstate-Mg2+. The exchange of cholesteryl esters between [C-14]cholesteryl ester-labeled LDL and unlabeled HDL was measured during a 16-h incubation, while LCAT was inhibited.

Results The addition of pravastatin to the diet induced a significant decrease in plasma **CETP** activity ($P < 0.05$); this effect was less evident in the group cotreated with vitamin E. For the first time, it was shown that **CETP** concentrations increased significantly after vitamin E alone ($P< 0.05$). No significant differences in the plasma activity of LCAT were observed among the groups.

Conclusions Pravastatin reduced **CETP** activity, but not that of LCAT. Addition of vitamin E prevented the decrease in **CETP** activity and had no effect on LCAT activity. The mechanism responsible for these effects is unknown, but could involve the prevention of radical-induced damage to **CETP** by vitamin E. Coronary Artery Dis 9:257-264 (C) 1998 Lippincott-Raven Publishers.

L17 ANSWER 15 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:173590 The Genuine Article (R) Number: YY175. Effects of testosterone replacement on HDL subfractions and apolipoprotein A-I containing lipoproteins. Tan K C B (Reprint); Shiu S W M; Pang R W C; Kung A W C. QUEEN MARY HOSP, DEPT MED, POKFULAM RD, HONG KONG, HONG KONG (Reprint); QUEEN MARY HOSP, DEPT CLIN BIOCHEM, HONG KONG, HONG KONG; UNIV HONG KONG, DEPT MED, HONG KONG, HONG KONG. CLINICAL ENDOCRINOLOGY (FEB 1998) Vol. 48, No. 2, pp. 187-194. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0NE. ISSN: 0300-0664. Pub. country: HONG KONG. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB OBJECTIVES Gonadal steroids are important regulators of lipoprotein metabolism, The aims of this study were to determine the effects of a minimum effective dose of testosterone replacement on high density lipoprotein (HDL) subfractions and apolipoprotein (ape) A-I containing particles (lipoprotein (Lp)A-I and LpA-I:A-II) in hypogonadal men with primary testicular failure and to investigate the underlying mechanisms of these changes,

MEASUREMENTS Eleven Chinese hypogonadal men were started on testosterone enanthate 250 mg intramuscularly at 4-weekly intervals. HDL was subfractionated by density gradient ultracentrifugation and LpA-I was analysed by electro-immunodiffusion after 3, 6 and 12 weeks of **treatment**. Plasma **cholesteryl ester transfer protein** (**CETP**) activity and lipolytic enzymes activities in post-heparin plasma were measured to determine the mechanisms underlying testosterone-induced changes in HDL.

RESULTS The dosage of testosterone enanthate used in the present study

resulted in suboptimal trough testosterone levels. No changes were seen in plasma total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL-C,) apo a and apo(a) after 12 weeks. There was a drop in HDL3-C compared to baseline (0.82 +/- 0.17 mmol/l vs, 0.93 +/- 0.13, P < 0.01) whereas a small but significant increase was seen in HDL2-C (0.21 +/- 0.13 mmol/l vs. 0.11 +/- 0.09, P < 0.05). Plasma apo A-I decreased after **treatment** (1.34 +/- 0.25 particles (0.86 +/- 0.18 g/l vs. 0.99 +/- 0.24, P < 0.01). No changes were observed in the levels of LpA-I particles. No significant changes were seen in plasma **CETP** and lipoprotein lipase activities after testosterone replacement but there was a transient increase in hepatic lipase (HL) activity at weeks 3 and 6. The decrease in HDL correlated with the increase in HL activity (r = 0.62, P < 0.05).

CONCLUSIONS Testosterone replacement in the form of parenteral testosterone ester given 4-weekly, although unphysiological, was not associated with unfavourable changes in lipid profiles, The reduction in HDL was mainly in HDL3-C and in LpA-I:A-II particles and not in the more anti-atherogenic HDL2 and LpA-I particles. The changes in HDL subclasses were mainly mediated through the effect of testosterone on hepatic lipase activity.

L17 ANSWER 16 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:47647 The Genuine Article (R) Number: YQ039. The role of a common variant of the cholesterol ester transfer protein gene in the progression of coronary atherosclerosis. Kuivenhoven J A; Jukema J W; Zwinderman A H; deKnijff P; McPherson R; Bruschke V G; Lie K I; Kastelein J J P (Reprint).

UNIV AMSTERDAM, ACAD MED CTR, DEPT VASC MED, RM G1-123, MEIBERGDREEF 9, POB 22-700, NL-1105 AZ AMSTERDAM, NETHERLANDS (Reprint); UNIV AMSTERDAM, ACAD MED CTR, DEPT VASC MED, NL-1105 AZ AMSTERDAM, NETHERLANDS; UNIV AMSTERDAM, ACAD MED CTR, DEPT CARDIOL, NL-1105 AZ AMSTERDAM, NETHERLANDS; LEIDEN UNIV, DEPT CARDIOL, LEIDEN, NETHERLANDS; LEIDEN UNIV, DEPT BIOSTAT, LEIDEN, NETHERLANDS; LEIDEN UNIV, DEPT HUMAN GENET, NL-2300 RA LEIDEN, NETHERLANDS; OTTAWA HEART INST, LIPOPROT & ATHEROSCLEROSIS GRP, OTTAWA, ON, CANADA; INTERUNIV CARDIOL INST NETHERLANDS, UTRECHT, NETHERLANDS. NEW ENGLAND JOURNAL OF MEDICINE (8 JAN 1998) Vol. 338, No. 2, pp. 86-93. Publisher: MASS MEDICAL SOC. 10 SHATTUCK, BOSTON, MA 02115. ISSN: 0028-4793. Pub. country: NETHERLANDS; CANADA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background The high-density lipoprotein (HDL) cholesterol concentration is inversely related to the risk of coronary artery disease, The **cholesteryl ester transfer protein** (**CETP**) has a central role in the metabolism of this lipoprotein and may therefore alter the susceptibility to atherosclerosis.

Methods The DNA of 807 men with angiographically documented coronary atherosclerosis was analyzed for the presence of a polymorphism in the gene coding for **CETP**. The presence of this DNA variation was referred to as B1, and its absence as B2. All patients participated in a cholesterol-lowering trial designed to induce the regression of coronary atherosclerosis and were randomly assigned to **treatment** with either pravastatin or placebo for two years.

Results The B1 variant of the **CETP** gene was associated with both higher plasma **CETP** concentrations (mean [+/-SD], 2.29+/-0.62 mu g per milliliter for the B1B1 genotype vs. 1.76+/-0.51 mu g per milliliter for the B2B2 genotype) and lower HDL cholesterol concentrations (34+/-8 vs. 39+/-10 mg per deciliter). In addition, we

observed a significant dose-dependent association between this marker and the progression of coronary atherosclerosis in the placebo group (decrease in mean luminal diameter: 0.14+/-0.21 mm for the B1B1 genotype, 0.10+/-0.20 mm for the B1B2 genotype, and 0.05+/-0.22 mm for the B2B2 genotype). This association was abolished by pravastatin. Pravastatin therapy slowed the progression of coronary atherosclerosis in B1B1 carriers but not in B2B2 carriers (representing 16 percent of the patients taking pravastatin).

Conclusions There is a significant relation between variation at the **CETP** gene locus and the progression of coronary atherosclerosis that is independent of plasma HDL cholesterol levels and the activities of lipolytic plasma enzymes, This common DNA variant appears to predict whether men with coronary artery disease will benefit from **treatment** with pravastatin to delay the progression of coronary atherosclerosis. (C) 1998, Massachusetts Medical Society.

L17 ANSWER 17 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:384875 The Genuine Article (R) Number: ZN601. Lowering of serum **cholesteryl ester transfer protein** - But not lecithin:cholesterol acyltransferase - Activity levels by hypocholesterolemic drugs in the rabbit. Meijer G W (Reprint); Groener J E M; Beynen A C; VanTol A. UNILEVER RES LABS VLAARDINGEN, UNILEVER NUTR CTR, OLIVIER VAN NOORTLAAN 120, NL-3130 AC VLAARDINGEN, NETHERLANDS (Reprint); UNIV UTRECHT, DEPT LAB ANIM SCI, NL-3508 TD UTRECHT, NETHERLANDS; ERASMUS UNIV, DEPT BIOCHEM, CARDIOVASC RES INST, COEUR, NL-3000 DR ROTTERDAM, NETHERLANDS. CARDIOVASCULAR DRUGS AND THERAPY (MAR 1998) Vol. 12, No. 1, pp. 13-18. Publisher: KLUWER ACADEMIC PUBL. SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS. ISSN: 0920-3206. Pub. country: NETHERLANDS. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Cholesteryl ester transfer protein** (**CETP**) and lecithin:cholesterol acyltransferase (LCAT) are important factors in the regulation of serum lipoprotein metabolism. Rabbits were fed hypocholesterolemic drugs to investigate the effect on serum **CETP** and LCAT activity levels. The activities were assayed using exogenous substrate assays and are an estimate of **CETP** and LCAT mass. Groups of eight rabbits were fed a cholesterol-free diet containing either 0.03% simvastatin or 1% cholestyramine for 6 weeks. For comparison eight rabbits were fed a cholesterol-free control diet without drugs or a diet containing 0.1% cholesterol for 6 weeks. Total serum and lipoprotein triglyceride concentrations were not different after intervention with the hypocholesterolemic drugs or the cholesterol diet. Dietary cholesterol induced higher VLDL, IDL, and LDL cholesterol, as well as serum **CETP** activity, as expected. Serum LCAT activity showed Little change with intervention. Both simvastatin and cholestyramine tended to lead to decreased cholesterol in all lipoprotein fractions and caused a significant decrease in serum **CETP** activity when compared with the control diet. Both drugs also caused a significant lower LDL particle concentration, as judged from differences in LDL protein levels. Intervention with simvastatin or cholestyramine led to relatively cholesterol-poor LDL. These effects on LDL concentration and composition were opposite from the effects of cholesterol feeding. Differences in the cholesterol contents of VLDL and IDL were comparable with those in LDL. The results suggest that decreasing serum **CETP** activity levels by **treatment** with simvastatin or cholestyramine may contribute to lowering of cholesterol in apo B-containing lipoproteins. The effects are additional to the well-known increase in hepatic LDL receptor activity, which is likely to be the most important factor in LDL cholesterol lowering by these drugs.

L17 ANSWER 18 OF 22 MEDLINE DUPLICATE 3
97450950 Document Number: 97450950. PubMed ID: 9305883. Differential interaction of the human **cholesteryl ester transfer protein** with plasma high density lipoproteins (HDLs) from humans, control **mice**, and transgenic **mice** to human HDL apolipoproteins. Lack of lipid transfer inhibitory activity in transgenic **mice** expressing human apoA-I. Masson D; Duverger N; Emmanuel F; Lagrost L. (Laboratoire de Biochimie des Lipoproteines, INSERM CJF 93-10, Faculte de Medecine, 21033 Dijon Cedex, France.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Sep 26) 272 (39) 24287-93. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Plasma high density lipoproteins (HDLs) from humans, from transgenic **mice** to human apolipoprotein A-I (HuAITg **mice**), from transgenic **mice** to human apolipoprotein A-II (HuAIITg **mice**), from transgenic **mice** to human apolipoproteins A-I and A-II (HuAIAIITg **mice**), and from C57BL/6 control **mice** were isolated, and their ability to interact with the human **cholesteryl ester transfer protein** (**CETP**) was studied. Whereas cholesteryl ester transfer rates were gradually enhanced by the addition of moderate amounts of HDL from the different sources, striking differences appeared when HDL levels kept increasing beyond a maximal transfer value. Indeed, while a plateau value corresponding to maximal **CETP** activity was maintained when raising the concentration of HuAITg HDL and HuAIAIITg HDL, inhibitions could be observed with the highest levels of human, control **mouse** , and HuAIITg **mouse** HDL. The concentration-dependent inhibition of **CETP** activity could be reproduced by the addition of delipidated HDL apolipoproteins from control **mice**, but it was abolished by a 1-h preheating **treatment** at 56 degrees C. In contrast, no significant inhibition of **CETP** activity was observed with the delipidated protein moiety of HuAITg HDL, and cholesteryl ester transfer rates remained unchanged before and after a 1-h, 56 degrees C preheating step. Finally, the **CETP**-mediated transfer of radiolabeled cholesteryl esters from human low density lipoprotein to human HDL was significantly higher in the presence of lipoprotein-deficient plasma from HuAITg **mice** than in the presence of lipoprotein-deficient plasma from control **mice**. Interestingly, cholesteryl ester transfer rates measured with both control and HuAITg lipoprotein-deficient plasmas became remarkably similar following a 1-h, 56 degrees C preheating **treatment**. It is concluded that human, control **mouse**, and HuAIITg **mouse** HDL contain a heat-labile lipid transfer inhibitory activity that is absent from HDL of HuAITg and HuAIAIITg **mice**. Alterations in **CETP**-lipoprotein binding did not account for differential lipid transfer inhibitory activities.

L17 ANSWER 19 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
97:446723 The Genuine Article (R) Number: XC872. Interferon alpha induces disorder of lipid metabolism by lowering postheparin lipases and **cholesteryl ester transfer protein** activities in patients with chronic hepatitis C. Shinohara E (Reprint); Yamashita S; Kihara S; Hirano K; Ishigami M; Arai T; Nozaki S; KamedaTakemura K; Kawata S; Matsuzawa Y. OSAKA UNIV, SCH MED, DEPT INTERNAL MED 2, 2-2 YAMADAOKA, SUITA, OSAKA 565, JAPAN (Reprint). HEPATOLOGY (JUN 1997) Vol. 25, No. 6, pp. 1502-1506. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The effect of recombinant interferon alpha 2a (rIFN-alpha(2a)) on serum

lipoprotein metabolism was assessed in 39 patients with chronic viral hepatitis C. rIFN-alpha(2a) was administered intramuscularly at a dose of 9 x 10(6) U/d for 2 weeks and then for 3 times a week over 6 months. The serum cholesterol concentration significantly decreased one meek after rIFN-alpha(2a) administration. Approximately 67% of this decrease was attributed to the reduction of high-density lipoprotein (HDL)-cholesterol; a decrease in HD2-cholesterol was more evident. By contrast, serum triglyceride levels, largely derived from very-low density Lipoprotein (VLDL), significantly increased following rIFN-alpha(2a), **treatment**. Lipoprotein Lipase (LPL) and hepatic triglyceride lipase (HTGL) activities in the postheparin plasma were reduced by 75.7% and by 79.4%, respectively, and decreases in plasma **cholesteryl ester transfer protein** (**CETP**) activity and its protein mass were also observed. However, prothrombin time was ameliorated by rIFN-alpha(2a), suggesting that the decrease in LPL, HTGL, and **CETP** activities may not be due to a reduction in protein synthesis by the liver. Simple correlation analysis demonstrated that the changes in LPL activity before and after 2 weeks of **treatment** with rIFN-alpha(2a) showed a significant negative correlation with changes in serum triglyceride and VLDL-triglyceride and a positive correlation with changes in HDL-cholesterol and HDL2-cholesterol. These results suggest a major contribution of reduced LPL activity with regard to the lipoprotein disorders. In conclusion, rIFN-alpha(2a) **treatment** on patients with chronic hepatitis C causes marked changes in serum lipoprotein metabolism associated with decreases in LPL, HTGL, and **CETP** activities.

L17 ANSWER 20 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
96:142093 The Genuine Article (R) Number: TV417. ETHANOL-INDUCED REDISTRIBUTION OF **CHOLESTERYL ESTER TRANSFER PROTEIN** (**CETP**) BETWEEN LIPOPROTEINS. HANNUKSELA M L; RANTALA M; KESANIEMI Y A; SAVOLAINEN M J (Reprint). UNIV OULU, DEPT INTERNAL MED, KAJAANINTIE 50, SF-90220 OULU, FINLAND (Reprint); UNIV OULU, DEPT INTERNAL MED, SF-90220 OULU, FINLAND; UNIV OULU, BIOCTR OULU, SF-90220 OULU, FINLAND. ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY (FEB 1996) Vol. 16, No. 2, pp. 213-221. ISSN: 1079-5642. Pub. country: FINLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Since alcohol drinking reduces the concentration and activity of plasma **cholesteryl ester transfer protein** (**CETP**), we investigated the effects of alcohol on its synthesis and secretion by perfusing rabbit livers for 4 hours in the absence or presence of ethanol. The quantity of **CETP** mRNA in the perfused livers did not differ between the control and ethanol (25 mmol/L or 50 mmol/L) perfusions. **CETP** activity was determined by incubating [H-3]cholesteryl ester-labeled human LDL and unlabeled human HDL with the perfusion medium after removing the endogenous VLDL (secreted by the perfused liver) by ultracentrifugation. **CETP** activity in the perfusion medium increased at a linear rate that was not affected by ethanol. When the VLDL was removed by precipitation with polyethylene glycol or a heparin-Sepharose column instead of ultracentrifugation, practically no **CETP** activity was detected in the ethanol perfusions, whereas these procedures did not affect **CETP** activity in the control perfusions. Inhibition of ethanol oxidation by 4-methylpyrazole resulted in **CETP** activity similar to that of the controls. We conclude that ethanol does not affect the synthesis or secretion of **CETP**, but its oxidation may alter the distribution of **CETP** in lipoproteins. **CETP** seems to be present in VLDL as well as in HDL, and since VLDL is more rapidly catabolized than

HDL, this may explain the low plasma **CETP** concentration associated with alcohol consumption.

L17 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2002 ACS
1995:592558 Document No. 123:7295 Transgenic **mice** expressing both human apolipoprotein B and human **CETP** have lipoprotein cholesterol distribution similar to that of normolipidemic humans.
Grass, David S.; Saini, Urmil; Felkner, Roland H.; Wallace, Racheal E.; Lago, William J. P.; Young, Stephen G.; Swanson, Mark E. (DNX Biotherapeutics, Inc., Princeton, NJ, 08540, USA). J. Lipid Res., 36(5), 1082-91 (English)
1995. CODEN: JLPRAW. ISSN: 0022-2275.
AB Transgenic **mice** expressing both human apolipoprotein (apo) B and human **cholesteryl esters transfer protein** (**CETP**) have been developed. When fed a normal **mouse** chow diet, the apoB/**CETP** double transgenic animals had threefold higher serum **CETP** activity than humans and had human apoB levels that were similar to those of normolipidemic humans. When compared with nontransgenic **mice**, the total serum cholesterol levels in the female apoB/**CETP** transgenic **mice**, the total serum cholesterol levels in the female apoB/**CETP** transgenic animals were increased significantly. Serum HDL cholesterol levels were decreased significantly in b.omega..tau..rho. male and female apoB/**CETP** transgenic animals. The percentages of the total cholesterol within the HDL, LDL, and VLDL fractions of the apoB/**CETP** animals were approx. 30%, 65%, and 5%, resp., similar to the distribution of cholesterol in the plasmas of normolipidemic humans.

L17 ANSWER 22 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
93:333345 The Genuine Article (R) Number: LD279. ADIPOSE-TISSUE **CHOLESTERYL ESTER TRANSFER PROTEIN** MESSENGER-RNA IN RESPONSE TO PROBUCOL **TREATMENT** - CHOLESTEROL AND SPECIES DEPENDENCE. QUINET E M; HUERTA P; NANCOO D; TALL A R; MARCEL Y L; MCPHERSON R (Reprint). UNIV OTTAWA, INST HEART, LAB H453, 1053 CARLING AVE, OTTAWA K1Y 4E9, ONTARIO, CANADA; MCGILL UNIV, LIPOPROT & ATHEROSCLEROSIS RES GRP, MONTREAL H3A 2T5, QUEBEC, CANADA; COLUMBIA UNIV COLL PHYS & SURG, DEPT MED, DIV MOLEC MED, NEW YORK, NY, 10032. JOURNAL OF LIPID RESEARCH (MAY 1993) Vol. 34, No. 5, pp. 845-852. ISSN: 0022-2275.
Pub. country: CANADA; USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Probucol **treatment** results in an increase in plasma concentrations of **cholesteryl ester transfer protein** (**CETP**) which may account, in part, for the effects of this agent on plasma concentrations of HDL cholesterol. We have examined the mechanism by which probucol increases plasma **CETP** and have determined the associated changes in the plasma distribution of high density lipoprotein (HDL) particles. Studies were carried out in nine hypercholesterolemic subjects and five normal volunteers. Probucol **treatment** resulted in a 31% increase in plasma concentrations of **CETP** and a 23% decrease in HDL cholesterol ($P < 0.01$). The plasma concentration of LpA-I decreased by 40% ($P < 0.01$) whereas no change occurred in the LpA-I/A-II subclass of HDL. Plasma **CETP** increased significantly by 1 week of therapy and remained stable over 10 to 14 weeks of therapy. In spite of the significant increase in plasma concentrations of **CETP**, the abundance of **CETP** mRNA in peripheral adipose tissue decreased markedly ($P < 0.001$). These results suggested that probucol may alter **CETP** synthesis in another tissue such as liver or, alternatively, may have other effects on **CETP** secretion into or catabolism out of the plasma pool. Further

studies were carried out in hamsters because, in this species, adipose tissue is a major site and liver is a negligible site for **CETP** synthesis. Hamsters were fed probucol with or without dietary cholesterol because this species was previously shown to respond to dietary cholesterol with an increase in adipose tissue mRNA levels and in plasma **CETP** concentrations, thus providing the opportunity to determine whether probucol would alter these parameters independently of the dietary cholesterol effect. When animals were fed a cholesterol-free diet, probucol had no effect on plasma concentrations of HDL-C or **CETP** or on adipose tissue **CETP** mRNA abundance. Addition of cholesterol to the diet (0.5% w/w) resulted in significant increases both in plasma **CETP** and in the level of **CETP** mRNA in adipose tissue. When probucol was incorporated into the cholesterol-rich diet, there was a further and significant increase in plasma **CETP** and adipose tissue mRNA abundance and a decrease in HDL cholesterol. The effect of probucol on **CETP** gene expression may be mediated by alterations in a putative regulatory pool of cellular cholesterol and may, in turn, depend on net transport of cholesterol to and from specific tissues via chylomicrons, low density lipoproteins, or other lipoproteins.

=> s thomas l?/au or rittershaus c?/au

L18 6860 THOMAS L?/AU OR RITTERSHAUS C?/AU

=> s l18 "CETP"

MISSING OPERATOR L18 "CETP"
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l18 and "CETP"

L19 20 L18 AND "CETP"

=> dup remove l19

PROCESSING COMPLETED FOR L19
L20 13 DUP REMOVE L19 (7 DUPLICATES REMOVED)

=> d l20 1-13 cbib abs

L20 ANSWER 1 OF 13 BIOSIS COPYRIGHT 2002 BIOSIS DUPLICATE 1
2001:517733 Document No.: PREV200100517733. Plasmid-based vaccine for treating atherosclerosis. **Thomas, Lawrence J. (1)**. (1) Easton, MA USA. ASSIGNEE: AVANT Immunotherapeutics, Inc.. Patent Info.: US 6284533 September 04, 2001. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 4, 2001) Vol. 1250, No. 1, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.
AB A plasmid-based vaccine is provided herein based on the combination of DNA segments coding for one or more B cell epitopes of cholesteryl ester transfer protein (**CETP**) and one or more broad range helper T cell epitopes. Administration of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or treatment

of atherosclerosis.

L20 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2002 BIOSIS DUPLICATE 2
2001:298985 Document No.: PREV200100298985. An extended toxicologic evaluation
of an immunoneutralizing vaccine to produce anti-**CETP** antibodies for the prevention/treatment of atherosclerosis. **Thomas, Lawrence J. (1)**; Picard, Michele D. (1); Miller, David P. (1); Emmett, Constance D. (1); Scesney, Susanne M. (1); Pisano, Milissa L. (1); Adari, Hedy (1); Hammond, Russell A. (1); Marsh, Henry C. (1); **Rittershaus, Charles W. (1)**; Pettey, Carolyn L. (1). (1) AVANT Immunotherapeutics, 119 Fourth Ave., Needham, MA, 02494 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A566. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB A toxicology study was conducted with an immunoneutralizing vaccine designed to elicit antibodies that would bind to and block the function of
cholesteryl ester transfer protein (**CETP**), in order to prevent atherosclerosis. The vaccine consisted of a dimer of a 31 a.a. synthetic chimeric peptide containing an N-terminal cysteine, a T cell epitope (residues 830-843 of tetanus toxin), and a B cell epitope (residues 461-476 of human **CETP**), formulated with an alum adjuvant. In this study NZW rabbits were immunized with either 0 mg (4 males and 4 females), 0.1 mg (2 males and 2 females), 0.25 mg (4 males and 4 females) or 1.0 mg (4 males and 4 females) of the vaccine on days 1, 29 and 57. On day 197 (at a relative antibody minimum) half of the animals from groups 1, 3 and 4 were sacrificed. The remaining animals were reboosted and euthanized on day 211, at an expected antibody maximum. Blood samples were
taken periodically throughout the study and were assessed for hematology, clinical chemistry, and antibody titers. All rabbits in the non-control groups developed anti-rabbit **CETP** antibody titers, thus validating the immunogenicity of the vaccine. In all other measurements the vaccinated groups were indistinguishable from the control group. All animals were monitored for clinical abnormalities throughout the study, and at necropsy, gross pathology was assessed, selected organs were weighed, and samples of 44 tissues were taken for histopathology. By all the above parameters, no significant test article-related pathology was observed. This study demonstrated the administration of this **CETP** immunoneutralizing vaccine produced specific self-reactive antibody titers
but no detectable test article-related pathology.

L20 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2002 ACS
2002:4125 An immunotherapeutic approach for the treatment of low plasma HDL-Cholesterol. Ryan, Una S.; **Rittershaus, Charles W.** (AVANT Immunotherapeutics, Inc., Needham, MA, 02494-2725, USA). NATO Science Series, Series I: Life and Behavioural Sciences, 330(Vascular Endothelium), 26-33 (English) 2001. CODEN: NSSSC9. ISSN: 1566-7693. Publisher: IOS Press.

AB One determinant of plasma HDL-Cholesterol concn. is cholesteryl ester transfer protein (**CETP**) activity. Inhibition of **CETP** activity increases plasma HDL-C, thus providing a potential therapeutic target for the treatment of atherosclerosis. Using a vaccine approach, we
immunized New Zealand White rabbits with a peptide contg. a region of **CETP** known to be required for neutral lipid transfer function. **CETP**-vaccinated rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile compared with control rabbits. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher, and the fraction

of plasma cholesterol in LDL was 24% lower in the **CETP** -vaccinated group compared with the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits compared with controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP**, and support the concept that inhibition of **CETP** activity in vivo can be anti-atherogenic. Currently, this vaccine is in clin. trials.

L20 ANSWER 4 OF 13 MEDLINE DUPLICATE 3
2000482102 Document Number: 20436374. PubMed ID: 10978256.
Vaccine-induced antibodies inhibit **CETP** activity in vivo and reduce aortic lesions in a rabbit model of atherosclerosis. **Rittershaus C W**; Miller D P; **Thomas L J**; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (2000 Sep) 20 (9) 2106-12. Journal code: B89; 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.

AB Using a vaccine approach, we immunized New Zealand White rabbits with a peptide containing a region of cholesteryl ester transfer protein (**CETP**) known to be required for neutral lipid transfer function. These rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits than in controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP** and support the concept that inhibition of **CETP** activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L20 ANSWER 5 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
2000:559012 The Genuine Article (R) Number: 313NH. Toxicologic evaluation of an immunoneutralizing vaccine to produce anti-**CETP** antibodies for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Picard M D; Miller D P; Emmett C D; Scesney S M; Adari H; Hammond R A; Levin J L; Ryan U S; Marsh H C; Pettey C L; **Rittershaus C W**. AVANT IMMUNOTHERAPEUT INC, NEEDHAM, MA 02494. FASEB JOURNAL (11 MAY 2000) Vol. 14, No. 8, pp. 262-262. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L20 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2002 ACS
1999:282118 Document No. 130:310673 Xenogeneic cholesteryl ester transfer protein (**CETP**) for modulation of **CETP** activity in treatment of atherosclerosis. **Rittershaus, Charles W.**; **Thomas, Lawrence J.** (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.

AB Methods for modulating cholesteryl ester transfer protein (**CETP**)

activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based vaccine for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

L20 ANSWER 7 OF 13 BIOSIS COPYRIGHT 2002 BIOSIS DUPLICATE 4
1999:282999 Document No.: PREV199900282999. A vaccine to produce anti-cholesteryl ester transfer protein (**CETP**) antibodies for the prevention/treatment of atherosclerosis. **Thomas, L. J. (1)**; Picard, M. D. (1); Miller, D. P. (1); Honan, C. M. (1); Adari, H. (1); Emmett, C. D. (1); Marsh, H. C. (1); Ryan, U. S. (1); Pettey, C. L. (1); **Rittershaus, C. W. (1)**. (1) Avant Immunotherapeutics, Inc., Needham, MA, 02494 USA. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A693. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April
17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L20 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:762763 The Genuine Article (R) Number: 121HC. Use of xenogeneic cholesteryl ester transfer protein (**CETP**) in a plasmid-based vaccine to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Adari H; Picard M D; Honan C M; Miller D P; **Rittershaus C W**; Pettey C L. T CELL SCI INC, NEEDHAM, MA. FASEB JOURNAL (17 MAR 1998) Vol. 12, No. 4, Part 1, Supp. [S], pp. 1805-1805. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L20 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2002 BIOSIS
1998:200178 Document No.: PREV199800200178. Use of xenogeneic cholesteryl ester transfer protein (**CETP**) in a plasmid-based vaccine to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis. **Thomas, L. J.**; Adari, H.; Picard, M. D.; Honan, C. M.; Miller, D. P.; **Rittershaus, C. W.**; Pettey, C. L.. T Cell Sciences Inc., Needham, MA USA. FASEB Journal, (March 17, 1998) Vol. 12, No. 4, pp. A310. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L20 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2002 ACS
1997:740308 Document No. 128:10315 Plasmid-based vaccine for treating atherosclerosis. **Thomas, Lawrence J.** (T Cell Sciences, Inc., USA; Thomas, Lawrence J.). PCT Int. Appl. WO 9741227 A1 19971106, 66 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ,
DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US7294 19970501. PRIORITY: US 1996-640713 19960501; US 1997-802967 19970221.
AB A plasmid-based vaccine is provided that is based on the combination of DNA segments coding for one or more B cell epitopes of **CETP** and one or more broad range helper T cell epitopes. Administration of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or treatment of atherosclerosis.

L20 ANSWER 11 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
97:166073 The Genuine Article (R) Number: WH142. A plasmid-based vaccine to elicit autoantibodies to cholesteryl ester transfer protein (**CETP**) for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Picard M D; Stewart S E; WAite B C D; Lin A Y; **Rittershaus C W**; Pettey C L. T CELL SCI INC, NEEDHAM, MA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (JAN 1997) Vol. 99, No. 1, Part 2, Supp. [S], pp. 754-754. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: USA
. Language: English.

L20 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2002 BIOSIS
1997:144273 Document No.: PREV199799443476. A plasmid-based vaccine to elicit autoantibodies to cholesteryl ester transfer protein (**CETP**) for the prevention/treatment of atherosclerosis. **Thomas, L. J.**; Picard, M. D.; Stewart, S. E.; Waite, B. C. D.; Lin, A. Y.; **Rittershaus, C. W.**; Pettey, C. L.. T Cell Sci. Inc., Needham, MA USA. Journal of Allergy and Clinical Immunology, (1997) Vol. 99, No. 1 PART 2, pp. S187. Meeting Info.: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997 ISSN: 0091-6749. Language: English.

L20 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2002 ACS
1997:12606 Document No. 126:46315 Modulation of cholesteryl ester transfer protein (**CETP**) activity. **Rittershaus, Charles W.**; **Thomas, Lawrence J.** (T Cell Sciences, Inc., USA; Rittershaus, Charles W.; Thomas, Lawrence J.). PCT Int. Appl. WO 9634888 A1 19961107, 81 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US6147 19960501. PRIORITY: US 1995-432483 19950501.
AB This invention relates to peptides comprising a helper T cell epitope portion and a B cell epitope portion for eliciting an immune response against endogenous cholesteryl ester transfer protein (**CETP**) activity, to prevent or treat cardiovascular disease, such as atherosclerosis. The T helper T cell epitope may be derived from an antigenic peptide selected from the group consisting tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacile Calmette-Guerin, polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein deriv. of tuberculin, keyhole limpet hemocyanin, hsp70 and combination thereof.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	225.51	225.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.53	-10.53

STN INTERNATIONAL LOGOFF AT 11:03:10 ON 15 JAN 2002